201-14924B

I U C L I D

D a t a S e t

New Chemical	ID: 2163-42-0
CAS No.	2163-42-0
Producer Related Part	
Company:	Lyondell Chemical Co.
Creation date:	11-JUN-2003
Substance Related Part	
Company:	Lyondell Chemical Co.
Creation date:	11-JUN-2003
Memo:	MPDiol HPV
Printing date:	02-DEC-2003
Revision date:	
Date of last Update:	**02-DEC-2003**
Number of Pages:	**104**
Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 Applicant and Company Information

Name: Lyondell Chemical Co.
Contact Person: Dr Marcy I Banton **Date:**
Street: One Houston Center, Suite 1600, 1221 McKinney Street
Town: Houston, Texas, TX 77010
Country: United States

26-NOV-2003

1.0.2 Location of Production Site, Importer or Formulator

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1.0.3 Identity of Recipients

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1.0.4 Details on Category/Template

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1.1.0 Substance Identification

IUPAC Name: 2-methyl-1,3-propanediol
Mol. Formula: C4 H10 O2
Mol. Weight: 90

Remark: ELINCS No. 412-350-5
26-NOV-2003

1.1.1 General Substance Information

Purity type: typical for marketed substance
Substance type: organic
Physical status: liquid
Purity: >= 98 - % w/w
Colour: Clear, colorless
Odour: Little or no odor

Reliability: (2) valid with restrictions
26-NOV-2003 (25) (26) (27)

1.1.2 Spectra

Type of spectra: other: UV-VIS absorption spectra

Method: The UV-VIS absorption spectrum of 0.6 mol/l MP Diol Glycol was determined under neutral (water), acidic (water:HCl; 0.1N) and alkaline (water:NaOH; 0.1N) conditions at 25 degrees C.

Method: OECD Guideline No. 101 (1981) UV-VIS absorption spectra

Result: Under neutral conditions, absorbance was present below 300 nm however no absorbance maxima could be determined.

Under acidic conditions, one absorbance maximum was determined at 209 nm with a molar absorption coefficient of 1.81 l/(mol x cm).

Under alkaline conditions, absorbance was present below 300 nm however no absorbance maxima could be determined.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

24-JUL-2003 (38)

1.2 Synonyms and Tradenames

MP Diol

Remark: Standard marketed product
Reliability: (2) valid with restrictions
Company literature

28-JUL-2003 (26) (27)

MP Diol LO

Remark: Low-odor product
Reliability: (2) valid with restrictions
Company literature

28-JUL-2003 (25)

1.3 Impurities

Purity type: typical for marketed substance
CAS-No: 149-31-5
EINECS-Name: 2-methyl-1,3-pentanediol
Contents: <= 2 - % w/w

28-JUL-2003 (27)

1.4 Additives

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1.5 Total Quantity

Remark: 2-Methyl-1,3-propanediol (CAS No. 2163-42-0) is manufactured by hydroformylation of allyl alcohol (2-propen-1-ol, CAS 107-18-6) with carbon monoxide and hydrogen to the intermediate hydroxymethylpropionaldehyde, followed by hydrogenation.

It is produced by Lyondell Chemical Company at sites in the US and the Netherlands, and marketed under the commercial trade name of MPDiol Glycol.

A second manufacturer of 2-methyl-1,3-propanediol, Dairen, operates in Taiwan.

The total annual production of 2-methyl-1,3-propanediol in the US and Europe is estimated to be 50 million pounds.

02-DEC-2003

1.6.1 Labelling

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1.6.2 Classification

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1.6.3 Packaging

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1.7 Use Pattern

Remark: 2-Methyl-1,3-propanediol (MPDiol Glycol) is used as a solvent glycol (~25%) in personal care products (neutralizer, emollient, emulsifier, and humectant) as well as in the manufacture of resins and coatings (~75%). In the latter application, the two primary hydroxyl groups react with acids and acid anhydrides to yield polyesters.

2-Methyl-1,3-propanediol (MPDiol® Glycol) polyesters formed by the reaction of 2-methyl-1,3-propanediol with aromatic acids (isophthalic, terephthalic, and phthalic anhydride) result in hard, unsaturated polyester resins, which are used in applications such as bathroom countertops and tubs, as well as boat manufacture.

2-Methyl-1,3-propanediol (MPDiol® Glycol) polyester polyols, which are formed by reaction with acids such as adipic acid, are used in polyurethane formulations for the coatings industry.

02-DEC-2003

1.7.1 Detailed Use Pattern

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1.7.2 Methods of Manufacture

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1.8 Regulatory Measures

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1.8.1 Occupational Exposure Limit Values

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1.8.2 Acceptable Residues Levels

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1.8.3 Water Pollution

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1.8.4 Major Accident Hazards

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1.8.5 Air Pollution

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1.8.6 Listings e.g. Chemical Inventories

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1.9.1 Degradation/Transformation Products

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1.9.2 Components

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1.10 Source of Exposure

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1.11 Additional Remarks

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1.12 Last Literature Search

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1.13 Reviews

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2.1 Melting Point

Value: < -54 degree C

Method: Directive 84/449/EEC, A.1 "Melting point/melting range"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: The test substance was cooled from ambient temperature (approx. 20 degrees C) and the temperature recorded at intervals of 30 s. The test continued until the sample solidified.
Result: The viscosity of the sample increased as the temperature decreased without showing a clear phase transition from liquid to solid. At a temperature of 219 K (-54 degrees C) the stirrer inserted into the sample could not be moved.
Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark
Conclusion: The viscosity of the test substance increased with decreasing temperature until the sample solidified. No phase change (from liquid to solid) was detectable and hence no freezing point/freezing range could be determined.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
08-NOV-2003 (47)

2.2 Boiling Point

Value: = 212 degree C
Decomposition: no

Method: Directive 92/69/EEC, A.2
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Approx. 15 ml of test substance was placed in a distillation device fitted with a vigreux and heated in a silicone oil bath at atmospheric pressure. Boiling point was reached when the temperature just above the vigreux stabilized during heating.
Result: The stabilized temperature above the vigreux during boiling was 212 +/- 0.5 degrees C (mean and SD). There was no change in consistency of the sample, which remained a clear, colorless liquid.
Test substance: Identification: MP Diol Glycol

CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: The boiling point of MP Diol Glycol at room temperature is 212 +/- 0.5 degrees C (mean and SD) at 760 mm Hg.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

16-JUN-2003 (43)

2.3 Density

Type: relative density
Value: = 1.01 g/cm³ at 20 degree C

Method: Directive 84/449/EEC, A.3 "Relative Density"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: A glass pyncometer with a nominal volume of 10 ml was used, after calibration with Milli-Q water. The test was performed in duplicate at 20 +/- 0.5 degrees C.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: The density of MP Diol Glycol at 20 degrees C was 1.01 g/cm3.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

16-JUN-2003 (44)

2.3.1 Granulometry

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2.4 Vapour Pressure

Method: Directive 84/449/EEC, A.4 "Vapour pressure"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: The vapor pressure curve for MP Diol Glycol was determined in a closed system using the static process. A total of 125 data points were collected at 3 different temperatures (23.66, 29.87 and 36.11 degrees C).
Result: The test substance was considered to show ideal behavior, thus the vapor pressure was derived according to the method of Clarke and Glew (1966; Trans Faraday Soc., 62, 539).
Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark
Conclusion: The vapor pressure of MP Diol Glycol at 25 degrees C was calculated to be 2.8 +/- 0.1 Pa (mean and SD; equivalent to 2.1 +/- 0.2 x10^-2 mm Hg).
Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
16-JUN-2003 (15)

2.5 Partition Coefficient

Partition Coeff.: octanol-water
log Pow: = .24 at 20 degree C

Method: Directive 84/449/EEC, A.8 "Partition coefficient"
Year: 1993
GLP: yes

Method: 874 mg test substance was dissolved in 50.0 ml n-octanol (saturated with water). Three tests were performed with using different volumes of n-octanol and water (mutually saturated).

In the first test, the volumes of water and n-octanol were identical.

In the second and third test, volumetric ratios (n-octanol:water) of 1:1 and 2:1, respectively, were used.

The concentration of MP Diol Glycol in each phase was determined by GC (1,2-butanediol internal standard; limit of detection 2.5 x 10^-3% v/v) after mixing (5 min) and

separation (3500 x g). Each test was repeated in duplicate.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: The n-octanol/water partition coefficient for MP Diol Glycol was 0.24 +/- 0.03 (mean and SD) at 20 degrees C. The log Pow was -0.6.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

16-JUN-2003 (14)

2.6.1 Solubility in different media

Solubility in: Water
Value: >= 3000 mg/l at 25 degree C

Method: OECD Guide-line 105
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: 3.0 g test substance was mixed with 9.0, 3.0 or 1.0 ml double distilled water.

The test was performed at room temperature, and the resultant phases observed visually.

Result: A clear colorless liquid was obtained after mixing the test substance with double distilled water at ratios of 1:3, 1:1 or 3:1 (w/v).

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: MP Diol Glycol was completely miscible with double distilled water over the range over the range 1:3 to 3:1.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

08-NOV-2003 (16)

2.6.2 Surface Tension

Test type: Ring method
Value: = 72.2 mN/m at 20 degree C
Concentration: .996 g/l

Method: Directive 84/449/EEC, A.5
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: An aqueous solution of the test substance was prepared by dissolving 99.6 mg of MP Diol Glycol in 100 ml double distilled water.

A Kruss tensiometer (type K6) was used to measure the force required to withdraw a horizontally suspended ring from the surface of the test solution.

The measurement was repeated six times, and the mean corrected according to Harkins-Jordan (1930; J Am Chem Soc, 52, 1751).

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: The surface tension of a solution of MP Diol Glycol (0.996 g/l) was 72.2 mN/m, indicating that the substance is not surface active.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

08-NOV-2003 (48)

2.7 Flash Point

Value: = 127 degree C
Type: closed cup

Method: Directive 84/449/EEC, A.9 "Flash point"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: The test substance was placed in a Pensky-Martens closed flash point tester (DIN 51758) that was heated progressively (with stirring) until the vapor concentration in air was sufficiently high to support ignition. The test flame was applied to the vapor space above the sample every second. The test was performed in duplicate (rate of temperature

rise 2-3 degrees/min test 1; 1-2 degrees/min test 2).

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: The mean flash point (corrected for atmospheric pressure) was 127 degrees C at 101.3 kPa.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

17-JUN-2003 (46)

2.8 Auto Flammability

Value: = 380 degree C

Method: Directive 84/449/EEC, A.15 "Auto-flammability of volatile liquids or gases"

Year: 1993

GLP: yes

Test substance: as prescribed by 1.1 - 1.4

Method: In a preliminary experiment, the test substance was injected into a heated open 200 ml Erlenmeyer flask containing air. Heating commenced at 300 degrees C, and 20 ul MP Diol Glycol added by variable pipette into the vessel at increments of 20 degrees C. The contents were observed in a darkened room, and heating continued, until ignition occurred (400 degrees C).

In two definitive tests (each comprising triplicate determinations), the sample was heated to 400 degrees C and the temperature of the flask decreased (intervals of 2 degrees C) with simultaneous injection of 150 ul test substance.

Result: Self-ignition values of 380-402 degrees C were obtained for the two main tests (n=6 determinations; atmospheric pressure 1014 and 1010 hPa for test 1 and test 2, respectively).

Based on these findings, a self-ignition temperature of 380 degrees C (the lowest value obtained) was evident after injection of a 150 ul sample of MP Diol Glycol at 1010 hPa.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: MP Diol Glycol is auto-flammable, with a self-ignition temperature of 380 degrees C at 1010 hPa.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
17-JUN-2003 (42)

2.9 Flammability

Result: non flammable

Method: Directive 84/449/EEC, A.13 "Flammability (solids and liquids)"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: 5 ml of test substance was poured into a porcelain cup containing approx. 5 mm (depth) Celite 545 and mixed. The test apparatus was observed in a fume cupboard over 5 minutes at 19 degrees (actual test performed at room temperature). The test was repeated 6 times.
Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark
Conclusion: No ignition was observed. It was concluded that MP Diol Glycol is not highly flammable.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
17-JUN-2003 (45)

2.10 Explosive Properties

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2.11 Oxidizing Properties

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2.12 Dissociation Constant

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2.13 Viscosity

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2.14 Additional Remarks

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3.1.1 Photodegradation

DIRECT PHOTOLYSIS
Halflife t1/2: = 11.2 hour(s)

Method: other (calculated)

Remark: METHOD
AOPWin v1.90 in EPIWin v3.10 from the US-EPA and Syracuse Research Corporation, as described by Meylan and Howard (1993).

INPUT DATA
CAS No. 107-18-6

RESULTS
Estimated hydroxyl radical reaction rate constant = 11.424 E-12 cm3/molecule-sec

Based on this rate constant and the average atmospheric concentration of hydroxyl radicals*, the half-life of MPDiol is 11.2 hr.

* Footnote:
EPISuite uses an OH concentration of 1.5x10^6, which reflects an average concentration for 12 daylight hours. This is based upon:
- Leifer (1993) EPA/744/R-93/001 (NTIS PB93-149334), and
- Mount and Eisele (1992) Science 256, 1187-8.

Conclusion: Based on this rate constant and the average atmospheric concentration of hydroxyl radicals, the half-life of MP Diol is 11.2 hr.

Reliability: (2) valid with restrictions
Study performed according to accepted principles using US-EPA recommended model.

02-DEC-2003 (3) (28)

3.1.2 Stability in Water

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3.1.3 Stability in Soil

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3.2.1 Monitoring Data (Environment)

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3.2.2 Field Studies

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3.3.1 Transport between Environmental Compartments

Type: fugacity model level I
Method: other: Level 1 Mackay Fugacity Model Version 2.11, August 1999 (from http://www.trentu.ca/cemc/models.html).
Year: 2003
Air: .0058 **% (Fugacity Model Level I)**
Water: 99.97 **% (Fugacity Model Level I)**
Soil: .022 **% (Fugacity Model Level I)**

Method: INPUT DATA USED:
Molecular weight = 90
Data temperature = 25 degrees C
Log Kow = -0.6 (experimental)
Water solubility = 8.73E+05 g/m3 (calculated)
Vapor pressure = 2.8 Pa (experimental)
Melting point = -54 degrees C (experimental)
Result: The percentage environmental distribution calculated from the above parameters using the MacKay level 1 model is as follows:

Air = 0.0058%
Soil = 0.0222%
Water = 99.9714%
Fish = 1.26E-06%
Sediment = 4.94E-04%
Suspended Sediment = 1.54E-05%
Aerosol = 2.50E-07%

Test substance: As prescribed by 1.1 - 1.4
Conclusion: According to this model, MP Diol Glycol will concentrate mostly in water (>99.8%).
Reliability: (2) valid with restrictions
Accepted modeling method, based on reliable input data.
02-DEC-2003 (1)

Type: fugacity model level III
Method: other: EPI Suite v3.10
Year: 2003

Method: Melting Point (deg C): -54 (experimental)
Boiling Point (deg C): 212 (experimental)
Vapor Pressure (mm Hg): 0.021 (experimental)
Log Kow (octanol-water): -0.6 (experimental)

Default emissions of 1000 kg/h for air, water and soil (provided by EPI Suite v.3.10).
Result: Concentration (percent)
Half Life (hours)
Emissions (kg/hr/h)

Air
3.33
22.5
1000

Water
49.2
208
1000

Soil
47.4
208
1000

Sediment
0.0736
832
0

Henry's Law Constant
2.3E-007 atm-m3/mole
(EPI Suite v.3.10 estimate)

River
Lake

Water depth (meters)
1
1

Wind Velocity (m/sec)
5
0.5

Current velocity (m/sec)
1
0.05

HALF-LIFE (hours)
2418
2.645E+004

HALF-LIFE (days)
100.7
1102

HALF-LIFE (years)
0.2758
3.018

Test substance: As prescribed by 1.1 - 1.4

Conclusion: According to this model, assuming equal emission to air, water and soil, MP Diol Glycol will concentrate mostly in water (49.2%) and soil (47.4%).

It will require about 101 days to volatilize from a model river, and 1102 days to volatilize from a model lake.

Reliability: (2) valid with restrictions
Accepted modeling method, based on reliable input data.

26-NOV-2003 (1)

3.3.2 Distribution

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3.4 Mode of Degradation in Actual Use

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3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 10 mg/l related to Test substance
20 mg/l related to Test substance
Contact time: 28 day(s)
Degradation: >= 6 - 54 % after 28 day(s)
Result: other: degradation to carbon dioxide but criteria for ready biodegradability not met
Control Subst.: Acetic acid, sodium salt

Method: Directive 84/449/EEC, C.5 "Biotic degradation - modified Sturm test"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Source: fresh sludge from a municipal sewage treatment plant (Waterschap de Aa, Schijndel, The Netherlands)
Duration: 28 d
Test vessels: 3 l, brown glass bottles
Test volume: 30 ml
Replicates: 4
Nutrient medium: salts in reverse osmosis water (Milli-Q)
Aeration: Carbon dioxide-free air
Temperature: 20 +/- 2 degrees C
Test concentrations: 10 mg/l; 20 mg/l (nominal)
Positive control: sodium acetate, 20 mg/l
Blank control: inoculum without control or test substances
Collection of CO2: three carbon dioxide collection bottles (in series) containing 80 ml 0.25 N barium hydroxide

QUANTITATION OF CARBON DIOXIDE PRODUCTION
The amount of barium hydroxide remaining in the collection bottles was quantified by titration with 0.05 N HCl (phenolphthalein indicator; every other day for days 1-10, every 5th day on days 11-28).

DETERMINATION OF DISSOLVED ORGANIC CARBON
On day 26, the pH of the 4 test bottles was recorded and 1 ml concentrated HCl added to drive-off inorganic carbonate.

After overnight aeration samples were analyzed for Dissolved Organic Carbon (method not given).

DATA EVALUATION
The theoretical amount of carbon dioxide (ThCO2) that could be generated by MP Diol Glycol was calculated thus:
ThCO2 = [no. carbons in test substance x Mwt CO2]/Mwt MP Diol

Carbon dioxide production from MP Diol Glycol was calculated thus:
mg CO2 = [0.05 x ml HCl titrated]/2 x 44
and corrected for endogenous production of CO2.

ACCEPTABILITY CRITERIA
Results were considered valid if:
- at least 60% of the control substance (sodium acetate) had degraded within 28 d;
- total CO2 release in the blank at the end of the test was <50 mg CO2 per 3 liters medium

TOXICITY TEST
Since biodegradation of MP Diol Glycol was much less at 20 mg/l then at 10 mg/l, a supplemental toxicity test (40 mg/l sodium acetate in presence or absence of 20 mg/l MP Diol Glycol) was run (other conditions as above).

Result:

CARBON DIOXIDE PRODUCTION - MP Diol Glycol
Calculated ThOD = 1.96 mg CO2/mg MP Diol Glycol

Theoretical maximal production of carbon dioxide in test vessels:
- low concn: 58.8 mg (from 30 mg test substance in 3 l)
- high concn: 117.6 mg (from 60 mg test substance in 3 l)

CARBON DIOXIDE PRODUCTION - Positive control
Calculated ThOD = 1.073 mg CO2/mg sodium acetate

Theoretical maximal production of carbon dioxide in test vessels:
- 62.6 mg (from 58.3 mg positive control substance)

BIODEGRADATION
Significant degradation was detected in the vessels containing 10 mg/l MP Diol Glycol (54% at day 28).
Negligible degradation was detected at 20 mg/l MP Diol Glycol (6% at day 28).

Degradation of the positive control substance was 82% by the end of the test period. (Although degradation appeared to slow temporarily on days 10-20, the overall result was within the historic range for the laboratory and the test was considered valid.)

Total carbon dioxide release by the blank was 14 mg.

MONITORING
Temperature: range = 19.0-22.5 degrees C
pH:
- blank: 6.80
Positive control: 5.62
MP Diol Glycol (10 mg/l): 5.87
MP Diol Glycol (20 mg/l): 6.62

TOXICITY CONTROL
CO2 production in positive control (sodium acetate only) = 75.5 mg (theoretical = 86.4 mg)
CO2 production in toxicity control (sodium acetate + MP Diol Glycol) = 125 mg (theoretical = 165 mg)
The difference between the two values (50 mg CO2) can be related to degradation of MP Diol Glycol (theoretical = 79.2 mg)

Degradation of MP Diol Glycol in toxicity control = 63%.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: Although substantial degradation of MP Diol was recorded under the conditions of this test, the criteria for ready biodegradability were not met.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
09-NOV-2003 (7)

Type: aerobic
Inoculum: activated sludge, domestic
Concentration: 1 mg/l related to Test substance
3 mg/l related to Test substance
Degradation: = 15 - 64 % after 28 day(s)
Result: other: degraded at 3 mg/l but not 1 mg/l, criteria for ready biodegradability not met
Control Subst.: Acetic acid, sodium salt

Method: Directive 92/69/EEC, C.4-C
Year: 1998
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Source: fresh sludge from a municipal sewage treatment plant (Waterschap de Maaskant, 's-Hertogenbosch, The Netherlands)
Duration: experiment 1 = 35 d; experiment 2 = 56 d
Test vessels: 250-300 ml BOD bottles with glass stoppers
Test volume: 30 ml
Replicates: 2

Nutrient medium: salts in reverse osmosis water (Milli-Q)
Inoculum: 100 ul/l filtered secondary effluent
Test concentrations: 1 mg/l (low) or 3 mg/l (high), nominal
Temperature: 20-22 degrees C
pH: expt 1 = 7.6, expt 2 = 7.4
Positive control: sodium acetate, 2 mg/l
Blank control: inoculum without control or test substances
Toxicity control: test substance, reference substance, inoculum
Determination of O2 concentration: day 0 and days 3, 7, 10, 14, 17, 21, 24, 28, 35 and 56 (1 mg/l, expt 2 only)
Apparatus: WTW:OXI 530 dissolved oxygen meter, TriOxmatic EO 200 electrode

DATA EVALUATION
The measured BOD was corrected for endogenous oxygen demand recorded in the blank. The test substance was considered inhibitory if the oxygen depletion in the toxicity control was <75% of the sum of the positive control and low test substance concntration.

ACCEPTABILITY CRITERIA
Results were considered valid if:
- oxygen depletion in the blank did not exceed 1.5 mg/l after 28 d;
- residual O2 did not fall below 0.5 mg/l at any time;
- differences in O2 uptake between the replicates was <20% after 28 d;
- biodegradation of the reference substance was C.60% by d 14.

Result:

THEORETICAL OXYGEN CONSUMPTION
Calculated ThOD = 1.96 mg O2/mg MP Diol Glycol
ThOD sodium acetate = 0.78 mg O2 per mg

BIODEGRADATION, Experiment 1
Day 28:
- 26% degradation at 1 mg/l
- 64% degradation at 3 mg/l
Day 35:
- 43% degradation at 1 mg/l
- 62% degradation at 3 mg/l

BIODEGRADATION, Experiment 2
Day 28:
- 15% degradation at 1 mg/l
- 59% degradation at 3 mg/l
Day 35:
- 56% degradation at 3 mg/l
Day 56:
- 38% degradation at 1 mg/l

The positive control substance was degraded by > 60% within 3 d.

Oxygen depletion in the toxicity control was >75% of the sum

of the oxygen depletion of the positive control and the test substance (low), hence MP Diol was not inhibitory.

Temperature: expt 1 = 19.6-20.0 degrees C, expt 2 = 20.1-20.6
pH: 7.6, 7.4

Comment:
The study report notes that adaptation at 3 mg/l (7-10 d) was more rapid than at 1 mg/l (18 d or longer).

Test substance: Identification: MP Diol Glycol
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear colorless liquid
Batch No: SC 970619J05
Purity: >98%
Storage conditions: Room temperature in the dark
Specific gravity: 1.01

Conclusion: Although substantial degradation of MP Diol was recorded under the conditions of this test, the criteria for ready biodegradability were not met.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

16-NOV-2003 (17)

3.6 BOD5, COD or BOD5/COD Ratio

-

3.7 Bioaccumulation

BCF: = 3.16

Method: other: modeled data
Year: 2003

Remark: METHOD
BCFWin v2.14 in EPIWin v3.10 from the US-EPA and Syracuse Research Corporation, based on the methodology described in Meylan et al. (1999)

INPUT DATA USED:
CAS No. 2163-42-0
Log Kow = 0.24 (see Section 2.5 of this IUCLID dataset)

RESULTS
Estimated BCF = 3.162 (log BCF = 0.500)
MP Diol Glycol is not likely to bioaccumulate.

Conclusion: Based on results obtained from BCFWin v2.14, MP Diol is not likely to bioaccumulate.

Reliability: (2) valid with restrictions
Study performed according to accepted principles using US-EPA recommended model.

02-DEC-2003 (2) (29)

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 1000 - measured/nominal
LC50: > 1000 - measured/nominal
Limit Test: yes

Method: Directive 84/449/EEC, C.1 "Acute toxicity for fish"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS
Species: Cyprinus carpio (Linnaeus 1758), pathogen-free from a single parent
Source: Zodiac, Wageningen, The Netherlands
Mean length: 1.9 +/- 0.1 cm
Mean weight: 0.19 +/- 0.04 g
Feeding: no feeding during test period

CONDITIONS
Test type: static
Duration: 96 hr
Vessels: 3 l, all glass
Medium: ISO medium in reverse osmosis water (Milli-Ro)
Loading: 10 per vessel (0.6 g fish/l medium)
Replicates: 1 control vessel, 3 test vessels
Test concentrations: 1000 mg/l (limit test, based on rangefinder)
Aeration: continuous

PREPARATION OF TEST MEDIA
The test substance was added quantitatively to give a nominal final concentration of 1000 mg/l (no further details).

MONITORING
Mortality and other effects: at 5.5, 24, 48, 72 and 96 hr after the start of exposure
Dissolved oxygen: daily, all vessels
pH: daily, all vessels
Temperature: daily, one control vessel

ANALYSIS
Samples (10 ml, in duplicate) taken from each control and each test vessel at 0 and 96 hr for analysis by GC-FID

REFERENCE SUBSTANCE
The sensitivity of the test system was checked at 3-monthly

intervals using pentachlorophenol (0.0, 0.10, 0.18, 0.32, 0.56, 1.0 mg/l). Satisfactory results, consistent with historic laboratory data, were obtained.

STATISTICAL METHODS
No LC50 could be calculated because the test substance was non-toxic at 1000 mg/l.

Result: No mortality occurred in the preliminary test following 96 hr exposure to 0.1, 1.0, 10, 100 or 1000 mg/l.

Mean exposure concentration for samples taken from the three test vessels at the start of the test was 903, 876 and 893 mg/l and 938, 993 and 1007 mg/l at 96 hr.

No mortality was noted at any point in either control or test vessels in the main study.

pH varied from 8.0-8.2, oxygen concentration was >5mg/l for all measurements, temperature varied from 20.0-21.5 degrees C.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: Under the conditions of the investigation, the LC50 for MP Diol Glycol in Cyprinus carpio (carp) was greater than 1000 mg/l, the highest concentration tested.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

08-AUG-2003 (5)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 1000 - measured/nominal
EC50: > 1000 - measured/nominal
Limit Test: yes

Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS
Species: Daphnia magna (Straus)
Source: bred in-house
Age: < 24hr
Feeding: no feeding during test period

CONDITIONS
Test type: static
Duration: 48 hr
Vessels: 100ml, all glass
Medium: ISO medium in reverse osmosis water (Milli-Ro)
Loading: 10 per vessel
Test concentrations: 1000 mg/l (limit test, based on rangefinder)

PREPARATION OF TEST MEDIA
258.2 mg of MP Diol Glycol was mixed with 250 ml/SIO medium to give a final concentration of 1000 mg/l. The solution was divided between two vessels, each containing 100 ml.

MONITORING
Immobility: at 24 hr and 48 hr
pH, oxygen: at start and end of test (all vessels)
Temperature: daily in one control vessel, from 0 hr

ANALYSIS
Samples (10 ml, in duplicate) taken from each control and each test vessel at the start (0 hr) and end (48 hr) for analysis by GC-FID

REFERENCE SUBSTANCE
Potassium dichromate (0.0, 0.10, 0.18, 0.32, 0.56, 1.0, 1.8 mg/l). Satisfactory results, consistent with historic laboratory data, were obtained.

STATISTICAL METHODS
No LC50 could be calculated because the test substance was non-toxic at 1000 mg/l.

Result: No immobilization was noted in a preliminary test following

48 hr exposure to 0.1, 1.0, 10, 100 or 1000 mg/l.

Mean exposure concentrations of 1023 mg/l and 1032 mg/l were recorded in the main test at 0 hr and 48 hr, respectively.

No immobilization was noted in the main study at 24 hr or 48 hr in either the control or test vessels.

pH varied from 8.0-8.1, oxygen concentration was >8mg/l for all measurements, temperature varied from 20.5-21.0 degrees C.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: Under the conditions of the investigation, the EC50 for MP Diol Glycol in Daphnia magna (water flea) was greater than 1000 mg/l, the highest concentration tested.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

30-JUN-2003 (30)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: = 1000 - measured/nominal
EC10: - measured/nominal
EC50: > 1000 -
Limit Test: yes

Method: Directive 87/302/EEC, part C, p. 89 "Algal inhibition test"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST ORGANISMS
Species: Scenedesmus subspicatus (strain 86.81 SAG)
Source: in-house

CONDITIONS
Test type: static
Duration: 72 hr
Vessels: 100 ml, all glass
Test volume: 50 ml
Medium: ISO medium in reverse osmosis water (Milli-Q)
Loading: initial cell density 2x10^4 cells/ml

Replicates: 6 control, 3 per test concentration
Test concentrations: 0, 100, 180, 320, 560 and 1000 mg/l
Illumination: continuous (6000-8000 lux)
Aeration: continuous shaking

PREPARATION OF TEST MEDIA
A stock solution of 2 g MP Diol Glycol per liter ISO medium was diluted (ISO medium) to 200, 360, 640, 1120 and 2000 mg/l then mixed 1:1 with an equal volume of algal suspension.

MONITORING
Cell density: determined every 24 hr; microscopic chamber count (initial assessment) or spectrophotometric measurement at 720 nm (Lambda 1 spectrophotometer, Perkin Elmer).
pH: at beginning and end of test
Temperature: daily, one control vessel

ANALYSIS
Samples (10 ml, in duplicate) were taken from control, 100, 320 or 1000 mg/l vessels at 0 and 72 hr for analysis by GC-FID

REFERENCE SUBSTANCE
The sensitivity of the test system was checked at 3-monthly intervals using potassium dichromate (0.0, 0.10, 0.18, 0.32, 0.56, 1.0 mg/l). Satisfactory results, consistent with historic laboratory data, were obtained.

STATISTICAL METHODS
The average growth rate for exponentially growing cultures at each concentration was compared to the control value, and the percentage reduction in growth rate calculated. Williams test was used to test for statistical significance.

Result: No inhibition of algal growth was observed at any of the test concentrations used in the preliminary test.

ACHIEVED CONCENTRATION
Analytical results at zero time were variable, and returned mean values of 120, 361 and 873 mg/l for the 100, 320 and 1000 mg/l solutions, respectively. Mean analyzed results at 72 hr were 100, >383* and 1023 mg/l, respectively. Since the measured concentrations were +/- 20% of nominal, estimates of EC50 and NOEC values were based upon nominal values.
[* Note: value was greater than the highest calibration solution, taking 10-fold dilution factor into account.]

CELL GROWTH AND GROWTH RATE
Statistical analysis showed no significant inhibition of cell growth or reduction of growth rate at any concentration tested.

TEST CONDITIONS
pH increased from 8.5 at the start of the test to 8.5-8.6 at

72 hr. Temperature was 21 degrees C throughout the test period.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: Under the conditions of the investigation, MP Diol Glycol did not inhibit or reduce algal growth, hence both the nominal 72 hr EC50 for growth inhibition (EbC50) and the nominal EC50 for growth inhibition (ErC50) were both in excess of 1000 mg/l. The NOEC for both end-points was 1000 mg/l, the highest concentration tested.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

08-NOV-2003 (8)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: other: inhibition test
Species: activated sludge
Exposure period: 30 minute(s)
Unit: mg/l **Analytical monitoring:** no
NOEC: = 100 - measured/nominal
EC50: > 100 - measured/nominal

Method: Directive 88/302/EEC, C.11
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Source: fresh sludge from a municipal sewage treatment plant (Waterschap de Aa, Schijndel, The Netherlands)

Preparation of sludge: The sludge was sieved and washed with tap water. Approx. 250 ml was weighed and dried at 100-105 degrees C, and the dry weight used as a measure of mixed liquor suspended solids (MLSS; equivalent to 17.6 g/l). The sludge was stored overnight after addition of 50 ml synthetic sewage feed (peptone, meat extract and mixed salts) per liter, aerated and kept at 20 +/- 2 degrees C until use.

Duration: 30 min contact time
Test vessels: glass 300 ml oxygen bottles
Test volume: 500 ml (16 ml synthetic sewage feed, 200 ml activated sludge, 284 ml test/control substance in water)
Replicates: 2 control incubations, single test incubations
Temperature: 20 +/- 2 degrees C

Test concentrations: 0, 3.2, 10, 32, 50 or 100 mg MP Diol Glycol/l
Blank control: 284 ml water
Positive control: 3,5 dichlorophenol (0, 1, 3.2, 10, 32 or 50 mg/l)

DETERMINATION OF RESPIRATION RATE
Oxygen consumption was measured using a Tri Ox EO 2000 oxygen electrode with recorder.

ACCEPTABILITY CRITERIA
Results were considered valid if:
- the respiration rates of the controls were within 15% of one another;
- the IC50 of 3,5-dichlorophenol was in the accepted range of 5-30 mg/l

Result: TOXICITY OF MP DIOL GLYCOL
No inhibition of respiration was apparent at any concentration of MP Diol Glycol.

TOXICITY OF 3,5-DICHLOROPHENOL
Slight (7%) inhibition of respiration was apparent at 1 mg/l 3,5-dichlorophenol, increasing to 79.7% inhibition at 50 mg/l. The IC50 (determined by Probit analysis) was 12.1 mg/l.

STUDY ACCEPTABILITY
The mean respiration rates (45.55, 50.35 mg O2/l/hr) were within 15% of one another. The IC50 for 3,5-pentachlorophenol (12.1 mg/l) was within the acceptable range (5-30 mg/l).

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: The 30 minute IC50 for MP Diol Glycol toward activated sludge exceeded 100 mg/l. It was concluded that MP Diol Glycol was not toxic to aerobic waste-water bacteria.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

24-JUL-2003 (6)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

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4.5.2 Chronic Toxicity to Aquatic Invertebrates

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TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Sediment Dwelling Organisms

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4.6.2 Toxicity to Terrestrial Plants

Species: Lactuca sativa (Dicotyledon)
Endpoint: other: emergence, dry shoot wt
Unit: mg/kg soil dw
LC50: = 31 - 98

Method: OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Test species: Lactuca sativa var. Ithaca (lettuce)
Test soil: sandy loam, pH 5.6, from pasture land (Lot no. G2M800MO; Columbia, Missouri)
Test pots: plastic, 10x10x12 cm

TEST DESIGN
Pots were filled to the same approx. depth and planted with 10 seeds per pot, 1 pot per concentration and 4 replicates per concentration.

EXPOSURE CONCENTRATIONS
An aqueous stock solution was mixed with silica sand and then blended with test soil to give final concentrations of 0, 1, 10, 100 or 100 mg MP Diol Glycol/kg soil.

ENVIRONMENTAL CONDITIONS
Natural sunlight supplemented with 1000 watt high-pressure sodium grow lamps, 16 hr light, 8 hr dark. Light intensity was measured with a LI-COR Model LI-198 light meter with a quantum sensor. Humidity and temperature were recorded continuously. Plants were watered primarily from the bottom (some surface watering to prevent drying) using sub-irrigation trays.

OBSERVATIONS

Seedling emergence and phytotoxicity ratings were performed after 50% emergence of the control seedlings, and continued at weekly intervals. Phytotoxicity ratings were made on a scale of 0-100 (100=100% mortality).

STATISTICAL METHODS
The EC50 for emergence and shoot dry weight were estimated using the Trimmed Spearman-Karber method.

Remark: Results presented in report as mg/kg wet wt soil. Test report indicates that 13.3 kg soil was equivalent to 12.6 kg dry wt.

Corrected EC50 values:

Seedling emergence EC50 = 97.7 mg MP Diol/kg dry soil

Dry shoot weight EC50 = 30.6 mg MP Diol/kg dry soil

Result: Effect by treatment level: 0, 1, 10, 100 or 1000 mg MP Diol Glycol/kg soil

Percent emergence: 90, 90, 85, 63 and 5%
Percent post emergence survival: 94, 97, 96, 79, 25%
Phytotoxicity rating: 3, 3, 28, 28, 93
- stunting due to delayed emergence, reduced stand, necrosis and non-emergence
Shoot dry weight: 0, -3, -54, -48, -99%

Seedling emergence EC50 = 92.6 mg MP Diol/kg soil

Dry shoot weight EC50 = 29.0 mg MP Diol/kg soil

Test substance: Identification: MP Diol Glycol
Source: Lyondell Chemical Company Service Center Europe
Description: clear, colorless liquid
Batch No: RBMPD3727
Purity: 99.71%
Storage conditions: Room temperature

Conclusion: Under the conditions of the study, EC50 values of 31 and 98 mg MP Diol Glycol/kg dry soil were obtained in Lactuca sativa for emergence and shoot dry weight.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

08-NOV-2003 (24)

Species: Raphanus sativus (Dicotyledon)
Endpoint: other: emergence, dry shoot wt
Unit: mg/kg soil dw
EC50: = 811 - 1112

Method: OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Test species: Raphanus sativus (raddish)
Test soil: sandy loam, pH 5.6, from pasture land (Lot no. G2M800MO; Columbia, Missouri)
Test pots: plastic, 10x10x12 cm

TEST DESIGN
Pots were filled to the same approx. depth and planted with 5 seeds per pot, 2 pots per concentration, total of 40 seeds per concentration.

EXPOSURE CONCENTRATIONS
An aqueous stock solution was mixed with silica sand and then blended with test soil to give final concentrations of 0, 1, 10, 100 or 100 mg MP Diol Glycol/kg soil.

ENVIRONMENTAL CONDITIONS
Lighting: 16 hr light, 8 hr dark
Source: 1000 watt metal halide grow lamp.
Light intensity was measured with a LI-COR Model LI-198 light meter with a quantum sensor. Humidity and temperature were recorded continuously. Plants were watered primarily from the bottom (some surface watering to prevent drying) using sub-irrigation trays.

OBSERVATIONS
Seedling emergence and phytotoxicity ratings were performed after 50% emergence of the control seedlings, and continued at weekly intervals. Phytotoxicity ratings were made on a scale of 0-100 (100=100% mortality).

STATISTICAL METHODS
The EC50 for emergence and shoot dry weight were estimated using the Trimmed Spearman-Karber method.

Remark: Results presented in report as mg/kg wet wt soil. Test report indicates that 17.01 kg soil was equivalent to 15.3 kg dry wt.

Corrected EC50 values:

Seedling emergence EC50 = >1000 mg MP Diol/kg dry soil

Dry shoot weight EC50 = 811 mg MP Diol/kg dry soil

Result: Effect by treatment level: 0, 1, 10, 100 or 1000 mg MP Diol

Glycol/kg soil

Percent emergence: 98, 100, 100, 100, 100%
Percent post emergence survival: 100, 100, 100, 100, 80%
Phytotoxicity rating: 0, 0, 0, 0, 33
- slight stunting, some leaf cupping and curling, some leaf tip necrosis at 1000 mg/kg.
Shoot dry weight: 0, +1, +1, -5, -62%

Seedling emergence EC50 = >1000 mg MP Diol Glycol/kg soil

Dry shoot weight EC50 = 730 mg MP Diol Glycol/kg soil

Test substance: Identification: MP Diol Glycol
Source: Lyondell Chemical Company Service Center Europe
Description: clear, colorless liquid
Batch No: RBMPD3727
Purity: 99.71%
Storage conditions: Room temperature

Conclusion: Under the conditions of the study, EC50 values of 811 and 1112 mg MP Diol Glycol/kg dry soil were obtained in Raphanus sativus for emergence and shoot dry weight.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

08-NOV-2003 (24)

Species: Avena sativa (Monocotyledon)
Endpoint: other: emergence, dry shoot wt
Unit: mg/kg soil dw
EC50: = 1112 -

Method: OECD Guide-line 208 "Terrestrial Plants, Growth Test"
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Test species: Avena sativa (oats)
Test soil: sandy loam, pH 5.6, from pasture land (Lot no. G2M800MO; Columbia, Missouri)
Test pots: plastic, 10x10x12 cm

TEST DESIGN
Pots were filled to the same approx. depth and planted with 10 seeds per pot, 1 pot per concentration and a total of 40 seeds per concentration.

EXPOSURE CONCENTRATIONS
An aqueous stock solution was mixed with silica sand and then blended with test soil to give final concentrations of 0, 1, 10, 100 or 100 mg MP Diol Glycol/kg soil.

ENVIRONMENTAL CONDITIONS

Lighting: 16 hr light, 8 hr dark
Source: 1000 watt metal halide grow lamp.
Light intensity was measured with a LI-COR Model LI-198 light meter with a quantum sensor. Humidity and temperature were recorded continuously. Plants were watered primarily from the bottom (some surface watering to prevent drying) using sub-irrigation trays.

OBSERVATIONS
Seedling emergence and phytotoxicity ratings were performed after 50% emergence of the control seedlings, and continued at weekly intervals. Phytotoxicity ratings were made on a scale of 0-100 (100=100% mortality).

STATISTICAL METHODS
The EC50 for emergence and shoot dry weight were estimated using the Trimmed Spearman-Karber method.

Remark: Results presented in report as mg/kg wet wt soil. Test report indicates that 17.01 kg soil was equivalent to 15.3 kg dry wt.

Corrected EC50 values:

Seedling emergence EC50 = >1112 mg MP Diol/kg dry soil

Dry shoot weight EC50 = >1112 mg MP Diol/kg dry soil

Result: Effect by treatment level: 0, 1, 10, 100 or 1000 mg MP Diol Glycol/kg soil

Percent emergence: 98, 98, 100, 88, 80%
Percent post emergence survival: 100, 100, 100, 97, 96%
Phytotoxicity rating: 0, 0, 0, 0, 18
- slight leaf tip necrosis and stunting at 1000 mg/kg.
Shoot dry weight: 0, -9, -3, -16, -42%

Seedling emergence EC50 = >1000 mg MP Diol/kg soil

Dry shoot weight EC50 = >1000 mg MP Diol/kg soil

Test substance: Identification: MP Diol Glycol
Source: Lyondell Chemical Company Service Center Europe
Description: clear, colorless liquid
Batch No: RBMPD3727
Purity: 99.71%
Storage conditions: Room temperature

Conclusion: Under the conditions of the study, EC50 values 1112 mg MP Diol Glycol/kg dry soil were obtained in Avena sativa for emergence and shoot dry weight.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

08-NOV-2003 (24)

4.6.3 Toxicity to Soil Dwelling Organisms

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4.6.4 Toxicity to other Non-Mamm. Terrestrial Species

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4.7 Biological Effects Monitoring

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4.8 Biotransformation and Kinetics

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4.9 Additional Remarks

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5.0 Toxicokinetics, Metabolism and Distribution

In Vitro/in vivo: In vitro
Type: Metabolism
Species: rat

Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method:
ANIMALS
Animals: male and female SD rats, age 9-10 wk
Supplier: Charles-River, Wilmington, MA
Acclimation: 5 d
Diet: certified rodent diet No. 5002 (PMI Feeds Inc.), ad libitum
Water: tap water, ad libitum
Housing: group housed in suspended stainless steel cages
Environmental: 20.6-25.1 degrees C, 35.0-71.7% rel. humidity, 10-15 room air changes/hr.

IN VITRO STUDIES
Whole homogenate (post-700 g supernatant), a mitochondrial fraction (post-10,000 g pellet), a microsomal fraction (post 105,000 g pellet) and a cytosolic fraction (post 105,000 g supernatant) were prepared from livers and kidneys after homogenisation (Potter-Elvehjem tissue homogenizer) in 0.25 M sucrose in 0.1 M phopshate buffer containing EDTA, DTT and protease inhibitor. Samples were stored frozen at -70 degrees C until use.

NADH-depednent biotransformation of MP Diol by alcohol dehydrogenase (ADH) in tissue homogenates was quantified from the rate of formation of MP Diol-derived aldehyde metabolites after derivatization with 2,4-dinitrophenyl hydrazine (analysis by HPLC or LC-MS/MS). 4-methylpyrazole or disulfuram were added to some incubations.

Result:
Preliminary studies had shown that MP Diol was a good substrate for purified equine ADH.

In vitro incubations containing MP Diol, rat liver cytosol and NAD+ resulted in the formation of one major peak and two minor peaks (refered to as peaks 1, 2 and 3).

Addition of 4-methylpyrazole inhibited formation of all peaks while disulfuram was without effect.

The area response for peaks 1-3 in hepatic cytosol from female rats was 2-fold higher per mg protein when compared to the area response for male rat cytosol.

Barely-detectable metabolic activity was present in

mitochondrial and microsomal fractions from liver or kidney, and in kidney cytosol.

It was not possible to determine a definitive structure for the MP Diol-derived 2,4-DNP derivatives.

Test substance: MP Diol, CAS No 2163-42-0, >99% by GC-MS, Lyondell Chemical Co.

[2-14C]-MP Diol, 5.129 mCi/mmol, 107.4 uCi/g in sterile water, Lot 030305.

Conclusion: The results of these studies indicate that MP Diol is a substrate for rat liver alcohol dehydrogenase.

Reliability: (1) valid without restriction
Report available for review. Well reported GLP-compliant study.

09-NOV-2003 (4)

In Vitro/in vivo: In vivo
Type: Toxicokinetics
Species: rat
Doses, females: 100 or 1000 mg/kg bwt
Vehicle: water
Route of administration: gavage
Exposure time: 7 day(s)

Method: other: OECD 417; OPPTS CFR 870.7485
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS
Animals: female SD rats, age 9-12 wk
Supplier: Charles-River, Wilmington, MA
Acclimation: 5 d
Diet: certified rodent diet No. 5002 (PMI Feeds Inc.), ad libitum
Water: tap water, ad libitum
Housing: group housed in suspended stainless steel cages, individually housed in metabowls
Environmental: 20.6-25.1 degrees C, 35.0-71.7% rel. humidity, 10-15 room air changes/hr.

TREATMENTS
MP Diol in deionized water was administered by gavage at doses of 100 or 1000 mg/kg bwt (5 ml/kg bwt) to groups of 4 female rats, with each animal receiving approx. 10.5-13.0 uCi. The concentration and stability of the dosing solutions was confirmed by GC.

SAMPLE COLLECTIONS
Excreta (cooled on dry ice), cage rinse and expired carbon dioxide (trapped with NaOH) were collected at regular

intervals for up to 7 d. A preliminary study had found little excretion of 14C in exhaled air, hence this was excluded from the main investigation.

NECROPSY
Animals were sacrificed by exsanguination (vena cava) under carbon dioxide anaesthesia at study termination on day 7. Livers and kidneys were excised, weighed and stored frozen for subsequent radiochemical analysis. Carcasses were retained and solubilized.

MEASUREMENT OF RADIOACTIVITY
Radioactivity present in urine, cage wash and extracts from the air traps was quantified by direct liquid scintillation counting (LSC). Samples of feces, blood and tissues were oxidized, and carcass samples solubilized, prior to LSC.

ANALYSIS OF URINE
Aliquots of thawed urine were acidified, centrifuged and the supernatant analyzed by ion exclusion chromatography using HPLC with radiochemical flow detection. Glycol and carboxylic acid metabolites were quantified by GC after trimethylsilyl derivatization. Methyl ester derivatives were prepared after reaction with etheral diazomethane and subject to characterization by GC-MS, with emphasis on the presence of the R- and S-stereoisomers of methyl 3-hydroxyisobutyric acid.

Result:

ROUTES OF EXCRETION
Mass balance data demonstrated rapid elimination regardless of dose, with renal excretion and cage wash (approx. 31-45% of dose) and exhaled air (42-57%) predominating. Less then 1% of the dose was excreted in feces. Seven days post-dosing, 0.1% was present in blood, up to 0.3% in liver and kidney and around 5% retained in the carcass. The results are consistent with rapdi metabolism and elimination of metabolites in urine or as carbon dioxide.

RATE OF ELIMINATION
More than 60% of the dose was eliminated within 6 hr and 83% within 24 hr, regardless of dose. A further 5-6% was eliminated between days 1-6. The half-life for elimination was calculated as 3.57 hr (high dose) or 3.87 hr (low dose).

RENAL ELIMINATION
The bulk of radioactivity present in urine was recovered within 24 hr. Approx. 11% (low dose) or 30% (high dose) of the administered radiolabel was recovered after 6 hr, a furtehr 5-7% between 6-12 hr and 3-4% of the dose between 12-24 hr. The results were consistent with more rapid renal elimination of 14C during the first 6 hr after dosing with 1000 mg/kg bwt MP Diol.

QUANTITATION AND IDENTIFICATION OF RENAL METABOLITES
HPLC analysis with radioflow detection demonstrated the presence of 5 peaks in urine from female rats given 1000 mg/kg

bwt MP Diol and 4 peaks after administration of 100 mg/kg bwt. Two peaks, identified as C and E, predominated and accounted for the majority of products excreted:

	--------Peak C--------		--------Peak E-------	
	100 mg/kg	1000 mg/kg	100 mg/kg	1000 mg/kg
6 hr	8.4%	20.6%	6.2%	9.0%
12 hr	4.3	5.7	0.1	0.6
24 hr	2.8	2.4	0.0	0.0
48 hr	0.1	0.0	0.0	0.0

The other peaks (A, B, D) invividually accounted for <2% each of the material excreted between 0-24 hr.

GC-MS identified component C as the TMS-derivative of 3-hydroxybutyric acid (3HBA), and subsequently confirmed by a chemical database search. 3HBA was also identified following GC-MS analysis of methylated organic extracts of urine.

Peak E corresponded to TMS derivative of MP Diol, and was confirmed using authentic material.

Both substances were at a maximum in urine 6 hr post-treatment and diminished thereafter (only 3HBA detected at 24 hr, neither present thereafter).

Based upon relative retention times and on the results of spiking experiments with authentic diasteroisomers, the majority of 3HBA was identified as the R-stereoisomer (apporx. 85% as R-form, 15% in the S-form).

Test substance: MP Diol, CAS No 2163-42-0, >99% by GC-MS, Lyondell Chemical Co.

[2-14C]-MP Diol, 5.129 mCi/mmol, 107.4 uCi/g in sterile water, Lot 030305.

Conclusion: The results of these investigations demonstrate that MP Diol is rapidly metabolized and eliminated by the rat. The in vitro and in vivo analyses showed that metabolism was catalyzed by alcohol dehydrogenase (and possibly aldehyde dehydrogenase or other oxidases) to S- and R-stereoisomers of 3-hydroxybutyric acid and carbon dioxide. The portion of MP Diol converted to the R-stereoisomer of 3-HBA was the predomiant form excreted in urine.

Reliability: (1) valid without restriction
Report available for review. Well reported GLP-compliant guideline study.

09-NOV-2003 (4)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: other: limit test
Species: rat
Strain: Wistar
Sex: male/female
No. of Animals: 10
Doses: 5000 mg/kg bwt, undiluted
Value: > 5000 mg/kg bw

Method: other: Health Effects Test Guidelines, US EPA, August 1982
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals: Wistar rats (approx. 8 wk, males = 220-240g, females = 240-270g)
Supplier: Ace Animals, Boyerstown, PA
Dosing: single oral dose, 5000 mg/kg bwt, dosing needle
Observations: animals observed 1, 2 and 4 hr post-dose and twice daily thereafter for 14 d.
Necropsy: all animals subject to gross internal examination on day 14.

Result: Clinical observation:
Diarrhea, chromorhinorrhea and soiling of the anogential area were noted

Mortality:
All animals survived to scheduled necropsy

Necropsy findings:
Soiling of the anogential area and pink fluid in the bladder was noted in two animals, all others unremarkable.

Test substance: Identification: #A606630
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: not stated
Purity: not stated
Storage conditions: room temperature and humidity

Conclusion: Under the conditions of this study, the oral LD50 of MP Diol Glycol in male and female Wistar rats was >5000 mg/kg bwt.

Reliability: (1) valid without restriction
30-JUN-2003 (12)

5.1.2 Acute Inhalation Toxicity

Type: other: limit test
Species: rat
Strain: Wistar
Sex: male/female
No. of Animals: 5
Doses: 5100 mg/m^3
Exposure time: 4 hour(s)
Value: > 5100 mg/m³

Method: Directive 92/69/EEC;93/21/EEC, B.2
Year: 1997
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method:
Animals:
Wistar rats (Crl:[WI]WU BR; approx. 5-6 wk, males mean bwt = 292 g, females mean bwt = 195 g)

Study design:
5 males and 5 females exposed (nose only) to a nominal concentration of 5 g MP Diol Glycol/m^3 for 4 hr.

Generation of test atmosphere:
The test atmosphere was produced by nebulization of warmed sample of MP Diol Glycol. The apparatus was allowed to stabilize for 60 min prior to exposure of the animals. Particle size determinations (Lee (1972) Science, 567-575) demonstrated that 99.6-99.7% of the aerosol in the animals' breathing zone (duplicate determinations) had an aerodynamic diameter of 4.2 um or less. The MMAD was 2.4 um (SD 1.4).

Gravimetric analysis:
The concentration of test substance in the test atmosphere was determined by gravimetric analysis before, and 7 times during, exposure.

Nominal concentration:
The nominal concentration was determined by dividing the amount of MP Diol Glycol used by the total volume of air passed through the exposure unit. (Calculated to be 6.0 g/m^3, indicating a generation efficiency of 85%.)

Observations:
The rats were inspected before, during and after exposure and at least once daily for 14 d. Body weights were recorded on the day of exposure and 7 and 14 d post-exposure.

Necropsy:
All animals subject to gross internal examination on day 14.

Result: Gravimetric analysis showed that the average exposure concentration of MP Diol Glycol was 5100 +/- 200 mg/m^3.

One female exhibited a reduced respiration rate during the 4th hour of exposure. No treatment-related findings were apparent 1.5 hr or 14 d post-exposure. Body weights were unaffected by treatment.

Treatment-related findings at necropsy were limited to the lung and comprised thickened hyaline spots or small areas on all lobes from 3 males and all females. Small white areas were also apparent in one male.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Description: clear liquid
Lot No: SC 970619J05
Purity: >98%
Storage conditions: Room temperature, in the dark

Conclusion: Under the conditions of this study, the 4 hr inhalation LC50 of MP Diol Glycol in male and female Wistar rats was greater than 5100 mg/m^3.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

24-JUL-2003 (31)

5.1.3 Acute Dermal Toxicity

Type: other: limit test
Species: rabbit
Strain: other: New Zealand
Sex: male/female
No. of Animals: 10
Doses: 2000 mg/kg bwt, undiluted
Value: > 2000 mg/kg bw

Method: other: Health Effects Test Guidelines, US EPA, August 1982
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals: New Zealand albino rabbits (males = 2.0-2.7 kg, females = 2.2-2.7 kg)
Supplier: Ace Animals, Boyerstown, PA
Application site: dorsal area of the trunk (equivalent to approx. 10% of body surface) clipped free of fur 24 hr prior to application
Treatment: 2000 mg/kg bwt spread over application site, covered with gauze, held in place with non-irritating tape.
Exposure period: 24 hr
Body weights recorded pre-test, weekly and at termination.
Necropsy: all animals subject to gross internal examination on day 14.

Result: Clinical observation:
Diarrhea, yellow nasal discharge, few feces, bloated abdomen

and soiling of the anogential area were noted

Body weight
One male lost weight over the course of the study (5% decrease) and one female exhibited erratic weight gain (8% increase over 14 d). Mean male bwt increased from 2.4 kg at d 0 to 2.6 kg at d 14, while mean female body increased from 2.4 kg to 2.7 kg over the same period.

Mortality:
One female died on study day 12 with no abnormal predeath physical signs.

Necropsy findings:
Abnormalities of the lungs (congested, hemorrhagic), pleural cavity (excess fluid), liver (pale margins) and gastrointestinal tract (red areas, gas filled) were noted in the decedent animal.
Abnormalities of the kidney (dark areas) and gastrointestinal tract (distended with liquid, yellow contents) were noted in 3/9 survivors.
One animal had a tissue mass and hemorrhagic areas in the dorsal abdominal wall.

Test substance: Identification: #A606630
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: not stated
Purity: not stated
Storage conditions: room temperature and humidity

Conclusion: Under the conditions of this study, the dermal LD50 of MP Diol Glycol in male and female New Zealand rabbits was >2000 mg/kg bwt.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

16-NOV-2003 (9)

5.1.4 Acute Toxicity, other Routes

-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: undiluted
Exposure: Occlusive
Exposure Time: 24 hour(s)
No. of Animals: 6
Vehicle: other: none
PDII: 0
Result: not irritating
EC classificat.: not irritating

Method: other: Health Effects Test Guidelines, US EPA, August 1982
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals: New Zealand Albino rabbits (approx. 8 wk, 2-3 kg)
Supplier: Ace Animals, Boyerstown, PA
Test site: 2 intact, 2 abraded sites per rabbit
Application volume: 0.5 ml/site (total = 2 ml/rabbit)
Covering: plastic, held in place by tape
Observation time: 24, 48 and 72 hr post-application
Scoring: Draize methodology

Result: No erythema or edema was noted during the observation period.

No abnormal physical signs noted during the observation period.

Test substance: Identification: #A606630
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: not stated
Purity: not stated
Storage conditions: room temperature and humidity

Conclusion: Under the conditions of the test, MP Diol Glycol was not irritating to intact or abraded rabbit skin when applied under occlusion for 24 hr.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

29-JUN-2003 (11)

Species: human
Concentration: other: 50%, 100%
Exposure: Occlusive
Exposure Time: 14 day(s)
No. of Animals: 25
Result: not irritating

Year: 1997
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: SUBJECTS AND SELECTION CRITERIA
Twenty five subjects completed the study (male and female, age 18-70 yr). (An additional subject discontinued participation for personal reasons unrelated to exposure to the test substance.)

Selection criteria were:
- self-assessed sensitive skin
- willingness to cooperate
- absence of any visible skin disease or preexisting, potentially confounding, skin conditions;
- avoidance of topical and/or systemic steroids and/or antihistimines;
- reading, understanding and signing an Informed Consent Form;
- dependability and intelligence in following directions.

METHOD
Approx. 0.2 ml MP Diol (100%, 50% aqueous dilution) was applied to a 3/4"x3/4" gauze adhesive (occlusive) dressing (Kendall Healthcare Products Inc) places between the scapulae. The test substance was applied Monday-Friday, with the final patch left in palce until the following Monday, for a total of 14 consective days. The site was visually assessed prior to each patch application. Treatment was discontinued if a score of 3+ was obtained.

SCORING SYSTEM
0 = no visible reaction
1+ = mild erythema (faint, but definate pink)
2+ = well-defined erythema, possible mild edema
3+ = Erythema plus diffuse edema

Result: All treated areas remained normal throughout the test interval.
Test substance: MP Diol Lot SC950908P06
Conclusion: Under the conditions of the test MP Diol (100%, 50%) did not exhibit a potential for cumulative dermal irritation in 25 subjects with self-assessed sensitive skin.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant study.
09-NOV-2003 (18)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Exposure Time: 24 hour(s)
Comment: not rinsed
No. of Animals: 6
Vehicle: none
Result: not irritating
EC classificat.: not irritating

Method: other: Health Effects Test Guidelines, US
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals: New Zealand Albino rabbits (approx. 8 wk, 2-3 kg)
Supplier: Ace Animals, Boyerstown, PA
Test site: applied to one eye/rabbit, the other acting as a control
Application volume: 0.1 ml
Observation time: 24, 48 and 72 hr post-application
Scoring: Draize methodology
Result: All 6 treated eyes appeared normal, with no corneal, irridial or conjunctival reactions present.
Test substance: Identification: #A606630
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: not stated
Purity: not stated
Storage conditions: room temperature and humidity
Conclusion: Under the conditions of the test, undiluted MP Diol Glycol was not irritating to rabbit eye.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
29-JUN-2003 (10)

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Exposure Time: .5 minute(s)
No. of Animals: 3
Vehicle: none
Result: not irritating
EC classificat.: not irritating

Method: other: Health Effects Test Guidelines, US-EPA, August 1982
Year: 1988
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals: New Zealand Albino rabbits (approx. 8 wk, 2-3 kg)
Supplier: Ace Animals, Boyerstown, PA

Test site: applied to one eye/rabbit, the other acting as a control
Application volume: 0.1 ml
Washing: The eyes were washed with lukewarm water 20-30 s post-instillation
Observation time: 24, 48 and 72 hr post-instillation
Scoring: Draize methodology

Result: No corneal or irridial reactions were present, however slight conjunctival redness (score = 1) was present in 1/3 eye at 24 hr, fully resolved by 24 hr.

Test substance: Identification: #A606630
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: not stated
Purity: not stated
Storage conditions: room temperature and humidity

Conclusion: Under the conditions of the test, undiluted MP Diol Glycol was not irritating to rabbit eye after 20-30 s contact, with washing.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

30-JUN-2003 (10)

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Concentration 1st: Induction other: 10%
2nd: Challenge other: 25, 50 or 100%
No. of Animals: 20

Method: Directive 96/54/EC, B.6
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Animals: Himalayan albino guinea pigs (approx. 9 wk, 325-435 g)
Supplier: BRL Ltd, Basel, Switzerland
Control: n = 10
Test group: n = 20

PRELIMINARY STUDY
Objective: to identify concentrations of test substance for used in main study
Intradermal injection: 5%, 100% w/w evaluated
Topical application: 10%, 25%, 50%, 100% w/w evaluated

MAIN STUDY - INDUCTION PHASE
Intradermal injection:
Three pairs of i.d. injections were made at the margin of a 2x4 cm area of clipped scapular skin:
- 10% w/w MP Diol Glycol in physiological saline

- Freunds Complete Adjuvant 50% w/w in distilled water
- 10% w/w MP Diol Glycol in 50% aqueous Freunds Complete Adjuvant

Application of SDS:
Induction site clipped/shaved and 10% Sodium Dodecyl Sulfate w/w in petrolatum applied.

Topical induction:
0.5 ml undiluted MP Diol Glycol, under occlusion for 48 hr

Controls:
Treated as described above with omission of MP Diol Glycol.

MAIN STUDY - CHALLENGE PHASE
Hair was clipped/shaved from a 5x5 cm area on the left flank, and 0.5 ml of a solution of MP Diol Glycol applied (0% (distilled water), 25%, 50%, 100%) under occlusion for 24 hr. The test sites were assessed for redness and swelling 24 and 48 hr post-challenge. (The skin sites were re-shaved after the first reading.)

Result: INDUCTION
No erythema or edema was present 48hr after occluded dermal exposure.

CHALLENGE
Controls
No skin reactions present

Test group
Skin reactions were present as follows:
10%: 1 animal (#490), erythema grade 1, 24 and 48 hr post-challenge
50%: 1 animal (#490), erythema grade 1, 24 and 48 hr post-challenge; 2 animals (#489, #499) with erythema grade 1, 48 hr post challenge
100%: 1 animal (#490), erythema grade 1, 48 hr post challenge

No mortality or signs of systemic toxicity were noted.
Average bwt gain in treated animals was slightly greater than that of the controls.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: Slight redness (grade 1) was noted in 3/20 of the test group (15%) after challenge with 50% MP Diol Glycol. Applying the allergenicity rating of Kligman, MP Diol Glycol is considered to have a mild sensitizing potential in the

guinea maximization test.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.
08-NOV-2003 (13)

Type:	Patch-Test	
Species:	human	
Concentration 1st:	Induction	other: 0.2 ml, 50% aq. dilution occlusive epicutaneous
2nd:	Challenge	other: 0.2 ml, 50% aq. dilution occlusive epicutaneous
No. of Animals:	110	
Vehicle:	water	

Year: 1997
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: SUBJECTS AND SELECTION CRITERIA
One hundred and sixteen subjects (male and female, age 18-77 yr) were recruited for the study. One hundred and ten individuals completed the investigation. (The laboratory states that the remaining subjects discontinued their participation for various reasons unrelated to exposure to the test substance.)

Selection criteria were:
- absence of any visible skin disease or preexisting, potentially confounding, skin conditions;
- avoidance of topical and/or systemic steroids and/or antihistimines;
- reading, understanding and signing an Informed Consent Form;
- willingness to cooperate;
- dependability and intelligence in following directions.

INDUCTION PHASE
Approx. 0.2 ml of MP Diol Glycol (50% aq. dilution) was applied to a gauze pad (0.75" x 0.75") and applied to the upper mid-scapulae region of one hundred and ten male and female volunteers. The patch was covered with an occlusive dressing. The application procedure was repeated three times per week (Mon, Wed, Fri) for a total of 10 applications. The patches were removed after 24 hr (Tues, Thurs, Sat), and skin reactions evaluated 24 hr (Wed, Fri) or 48 hrs later (Mon), immediately prior to reapplication of the patch.

CHALLENGE PHASE
Two weeks after the 10th application, a challenge patch (50% aq. dilution) wasapplied to the original site and to the forearm (virgin site). These were removed after a 24 hr contact period, and reactions at the skin site assessed immediately and again after 24 hr (that is, 48 hr post-application). Any subject that showed a reaction was

re-examined 72 hr post-application and subsequently rechallenged with another patch.

Any subjects that responded on challenge were rechallenged 7 days later with neat and 50% diluted (water) MP Diol Glycol under occlusive and semi-occlusive conditions.

SCORING SYSTEM
0 = no visible reaction
1+ = mild erythema
2+ = well-defined erythema, possible barely perceptible oedema
3+ = Erythema and edema
4+ = Erythema and edema with vesiculation and ulceration

Result: Six subjects responded with skin reactions during induction and/or challenge.

INDUCTION
5 subjects (10, 45, 47, 48, 82) showed a mild (1+) reaction at some point during the induction phase.

Subject 10 responded on the 7th application only and at no other time point. Skin reactivity in subjects 45, 47 and 82 was not recorded until the 9th or 10th application (ie late in the induction phase of the study). Subject 82 responded on days 2-10 of the induction phase, possibly indicating an atopic response.

CHALLENGE
5 subjects (38, 45, 47, 48, 99) exhibited a skin response on at least one site on at least one time point during the challenge phase of the study.

Subject 38 showed a mild (1+) reaction 48 hr post-challenge at the original site, but this had resolved by 72 hr. No reaction was noted at the virgin site up to 72 hr post-challenge.

Subject 45 showed a mild reaction (1+) at 48 hr and 72 hr post-challenge at the original site, but no reaction at the virgin site up to 72 hr post-challenge.

Subject 47 showed a well defined (2+) reaction at the original site at 48 hr, which resolved to a mild reaction at 72 hr. The virgin site showed a mild reaction (1+) at both 48 hr and 72 hr.

Subject 48 showed a mild reaction (1+) at the original site at 48 hr and 72 hr, and at the virgin site at 72 hr only.

Subject 99 showed a Mild (1+) reaction at the original site at 48 hr and 72 hr, and a well defined-decreasing-to-mild reaction at the virgin site at 24-48 hr (2+) and 72 hr (1+).

RECHALLENGE 1
Subjects 45, 47, 48 and 99 participated in this phase of the study.

Subject 45 showed a mild (1+) reaction at the original and the virgin site to neat and diluted test substance, both under occlusion or semi-occlusion, at 48 hr but not at 24 hr.

Subject 47 showed a well defined (2+) reaction at 48 hr only when MP Diol Glycol was applied to the virgin site under occlusion, but not at any other site, time point or exposure condition.

Subject 48 showed a well defined (2+) or mild (1+) response to neat MP Diol Glycol under occlusion at the original and virgin sites, respectively, and a mild (1+) response at 48 hr only at the original site when semi-occluded. This individual showed no dermal reactivity to a 50% dilution under any exposure condition at any time point.

Subject 99 showed a mild (1+) response at the original site only 48 hr after rechallenge under occlusion. There was no reaction at the virgin site when occluded, nor was there any response at any time at the semi-occluded sites. (No rechallenge with diluted MP Diol Glycol was conducted with this subject).

RECHALLENGE 2
Subjects 38, 47 and 48 (ie those that showed a response on challenge with MP Diol Glycol) were rechallenged with propylene glycol and 1,3-butylene glycol, under occlusion.

Subject 38 showed a mild (1+) response to propylene glycol at the original MP Diol Glycol induction/challenge site. During a third rechallenge with MP Diol Glycol, no reaction was recorded at any site at any time.

Subject 47 showed a mild (1+) response to propylene glycol at 24 hr and 48 hr when applied to both original and the virgin sites, and a mild (1+) response to butylene glycol at both time points at the virgin site only.

Subject 48 showed well defined (2+) responses to both propylene glycol and butylene glycol at both sites and at all time points.

INTERPRETATION
The occurrence of a mild dermal response in 3 subjects on the 9th or 10th day of the induction phase of this study is indicative of either an irritant or allergic reaction. Skin reactions in another subject on days 2- 10 of the induction phase are suggestive of an atopic response.

Responses in 5 subjects during the challenge phase, although mild, were generally delayed and appeared between the 24 hr and 48 hr observation periods. Once established, these reactions persisted to 72 hr. Skin responses were noted at the virgin site in 2 subjects, with one of these showing a well defined reaction immediately after removal of the challenge patch. An irritant basis for these responses seems unlikely since there had been no contact with MP Diol in the 10 days preceding the challenge.

When 4 of the 'responders' were rechallenged with neat or 50% aqueous MP Diol Glycol, mild-well defined delayed reactions were noted at the 48 hr observation point after occluded application, but responses after semi-occluded application were less marked. The concentration MP Diol Glycol used in the challenge application had negligible effect on the magnitude of the response.

Similar responses were noted in 2 of the 3 'responders' after rechallenge with propylene- or butylene glycol under occlusion, with mild to well defined responses present from 24 hr post-application at both the original and the virgin sites.

There are several uncertainties and confounders in these data. Since no reaction during induction or challenge was noted for the majority of subjects, is clear that MP Diol Glycol is neither a strong irritant nor a strong sensitizer. However the mild-well defined responses seen in a handful of subjects indicates it has some potential, albeit weak, to elicit a dermal reaction. The delayed nature of this response tends to point towards an allergic response. However the occurrence of a delayed response after rechallenge with butylene glycol or propylene glycol mitigate against this conclusion, since neither are known sensitizers. It may be that these individuals were unrecognized atopics, and responded in an undefined manner to MP Diol, propylene and butylene glycols.

Test substance: No details.

Conclusion: Mild responses were seen in a small number of subjects under the occlusive application conditions seen in this study, however it is unclear if these are irritant or allergic in nature. The occurrence of a delayed response to 1,3-butylene glycol or propylene glycol in some of these individuals points to irritation or atopy as a possible basis for these reactions.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant study.

26-NOV-2003 (19)

Type: Patch-Test
Species: human
Concentration 1st: Induction other: 0.2 ml, 50% aq. dilution occlusive epicutaneous
2nd: Challenge other: 0.2 ml, 50% aq. dilution occlusive epicutaneous
No. of Animals: 104
Vehicle: water

Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Study identity: C99-0968.01

SUBJECTS AND SELECTION CRITERIA
One hundred and thirteen subjects (male and female, age 19-79 yr) were recruited for the study. One hundred and four individuals completed the investigation. (The laboratory states that the remaining subjects discontinued their participation for various reasons unrelated to exposure to the test substance.)

Selection criteria were:
- male and female subjects, age 16 and over;
- absence of any visible skin disease or preexisting, potentially confounding, skin conditions;
- prohibition of use of topical and/or systemic steroids and/or antihistimines for at least 7 d prior to study initiation;
- completion of a medical history form and the understanding and signing an Informed Consent Form;
- considered reliable and capable of following directions.

INDUCTION PHASE
Approx. 0.2 ml of test material (50% dilution in water) was applied to a gauze pad (0.75" x 0.75") and applied to the upper mid-scapulae region of one hundred and four male and female volunteers. The patch was covered with an occlusive dressing. The application procedure was repeated three times per week (Mon, Wed, Fri) for a total of 9 applications. The patches were removed after 24 hr (Tues, Thurs, Sat), and skin reactions evaluated 24 hr (Wed, Fri) or 48 hrs later (Mon), immediately prior to reapplication of the patch. (Note: Some individuals (nos. 1-45, panel 19990609) were induced initially with undiluted test material, but this was amended after the first application.)

CHALLENGE PHASE
Approx. two weeks after the final application, a challenge patch was applied to a virgin site, adjacent to the induction site. This was removed after a 24 hr contact period, and reactions assessed immediately and again 72 hr post-application. (Note : the concentration of the challenge

patch is not stated directly, but is presumed to be 50% in water).

SCORING SYSTEM
0 = no visible reaction
+ = barely perceptible or spotty erythema
1 = mild erythema covering most of the test site
2 = moderate erythema, possible presence of mild edema
3 = marked erythema, mild edema
4 = Severe erythema, possible edema, vesiculation, bullae and/or ulceration
(Note: this is not the same scoring system as that used in the earlier study, C97-0156)

Result: One subject (no. 18, panel 19990609) responded with varying degrees of erythema (barely perceptible to moderate) during all stages of the study. This was considered an irritant hypersensitivity reaction by the laboratory conducting the study. This subject is not included in the following evaluation of these data.

A second (no. 16, panel 19990609) responded with mild erythema (score 1) during induction phase 7 and 8 only, a third (no. 2, panel 19990625) with barely perceptible- or mild erythema on induction phase 2-9, while a fourth (no 8, panel 19990625) showed barely perceptible erythema on induction phase 6 and 7. None of these individuals showed reactions on challenge. Four other individuals responded with barely perceptible erythema (score +) on at least on occasion during the induction phase.

INTERPRETATION
Skin responses recorded in this study were consistent with sporadic, barely perceptible to mild irritation in 6 subjects during the induction phase of the study. No reaction was noted in a further 97 individuals after application under occlusion.

No response was elicited on challenge at a site previously unexposed to MP Diol Glycol.

The results indicate that 50% MP Diol Glycol was not a sensitizer under the conditions of the study, although it was minimally irritating in some individuals following repeated application.

Test substance: Low odor sample, no further details.

Conclusion: MP Diol Glycol was not a sensitiser under the occlusive conditions used in this study although minimal irritation was observed in some individuals.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant study.

26-NOV-2003 (22)

Type: Patch-Test
Species: human
Concentration 1st: Induction other: 0.2 ml, 50% aq. dilution occlusive epicutaneous
2nd: Challenge other: 0.2 ml, 50% aq. dilution occlusive epicutaneous
No. of Animals: 104
Vehicle: water

Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Identical methodology to previous entry (C99-0968.01).
Result: One subject (no. 18, panel 19990609) responded with varying degrees of erythema (barely perceptible to marked) on induction days 0 - 5, and treatment was suspended. On challenge, this individual showed mild erythema 24 hr post-challenge, and barely perceptible erythema 72 hr and 96 hr post-challenge. This was considered an irritant hypersensitive reaction by the contract house. This subject is not included in the following evaluation of these data.

Some subjects showed a barely perceptible response (score +) on one (n = 3) or two (n = 1) occasions during the induction period.

Subject 16 (panel 19990609) showed mild erythema (score 1) on induction phases 7 and 8, while subject 2 (panel 19990625) showed a barely perceptible response (score +) on induction phase 4, and a mild response (score 1) on induction phases 5-8.

One subject (no. 33, panel 19990625) showed a barely perceptible response (score +) on challenge (72 hr and 96 hr time points), but had no reaction during induction.

INTERPRETATION
Skin responses recorded in this study were consistent with sporadic, barely perceptible to mild irritation in six subjects during the induction phase, while a seventh showed a barely perceptible response on challenge only. No reaction was noted in a further 96 individuals.

The results indicate that a 50% dilution of MP Diol Glycol was not a sensitizer under the conditions of the study, although it was minimally irritating in some individuals following repeated exposure.
Test substance: No details.
Conclusion: MP Diol Glycol was not a sensitizer under the occlusive conditions used in this study although minimal irritation was observed in some individuals.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant study.

26-NOV-2003 (20)

Type: Patch-Test
Species: human
Concentration 1st: Induction other: 0.2 ml, 50% aq. dilution semiocclusive
2nd: Challenge other: 0.2 ml, 50% aq. dilution semiocclusive
No. of Animals: 104
Vehicle: water

Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Study identity: C99-0968.02

Methodology similar to preceding study (C99-0968.01) with the following exceptions :
- a larger gauze pad was used for application of the sample (1" x 1")
- gauze was held in place by a semi-occlusive adhesive dressing

Result: One subject (no. 18, panel 19990609) responded with varying degrees of erythema (barely perceptible to moderate) on induction phases 4 - 9, and with mild erythema 24 hr after challenge. This was considered an irritant hypersensitive reaction by the contract house. This subject is not included in the following evaluation of these data.

Another subject (no. 2, panel 19990625) responded with barely perceptible erythema (score +) on induction phase 1 to 3, and with mild erythema (score 1) on induction phase 4 to 9. This individual showed a barely perceptible (score +) skin reaction 72 hr after challenge, but this had resolved (score 0) 24 hr later.

Four other individuals showed a single, barely perceptible response on one occasion during the induction phase, and one of these (no. 2, panel 19990625) showed a barely perceptible skin reaction 72 hr and 96 hr post-challenge.

INTERPRETATION
Skin responses recorded in this study were consistent with sporadic, barely perceptible to mild irritation in five subjects during the induction phase of the study. No reaction was noted in ninety eight individuals after application under semi-occlusion.

With the exception of the single subject mentioned above (no. 2, panel 19990625), no response was elicited on challenge at a site previously unexposed to MP Diol Glycol.

The results indicate that 50% MP Diol Glycol was not a sensitizer under the conditions of this study, although it was minimally irritating following repeated application.

Test substance: Low odor sample, no further details.
Conclusion: MP Diol Glycol was not a sensitizer under the semiocclusive conditions used in this study although minimal irritation was observed in some individuals.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant study.
26-NOV-2003 (23)

Type: Patch-Test
Species: human
Concentration 1st: Induction other: 0.2 ml, 50% aq. dilution semiocclusive
2nd: Challenge other: 0.2 ml, 50% aq. dilution semiocclusive
No. of Animals: 104
Vehicle: water

Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: Identical methodology to previous entry (C99-0968.02).
Result: One subject (no. 18, panel 19990609) responded with varying degrees of erythema (barely perceptible to marked) on induction phase 0, and again on induction phases 3 and 4, at which time induction was suspended. The subject also showed a mild to moderate skin reaction on challenge, which persisted to 96hr. These responses were considered indicative of irritant hypersensitivity by the contract house. This subject is not included in the following evaluation of these data.

Three subjects showed a barely perceptible response (score +) on one occasion during the induction period, and one of these individuals responded with a barely perceptible response (score +) at 72 and 96 hr post-challenge.

Subject 2 (panel 19990625) showed a barely perceptible response (score +) on induction phases 2 - 4, and a mild response on induction phases 5 - 8. This individual also showed a barely perceptible response (score +) 72 hr post-challenge only (clear at 96 hr).

INTERPRETATION
Skin responses recorded in this study were consistent with sporadic, barely perceptible to mild irritation in three subjects, and a slightly more sustained response in a fourth, during the induction phase of the study. Two of these four showed a barely perceptible response (score +) on challenge. No reaction was noted in a further 99 individuals after application under semi-occlusive conditions.

The results indicate that MP Diol Glycol was not a sensitiser under the conditions of the study, although it was minimally irritating in some individuals following repeated application.

Test substance: No details.
Conclusion: MP Diol Glycol was not a sensitiser under the semiocclusive conditions used in this study although minimal irritation was observed in some individuals.
Reliability: (1) valid without restriction
Report available for review. GLP-compliant study.
26-NOV-2003 (21)

5.4 Repeated Dose Toxicity

Type: Sub-acute
Species: rat **Sex:** male/female
Strain: Wistar
Route of administration: gavage
Exposure period: 14 d
Frequency of treatment: daily
Doses: 0, 300, 600 or 1000 mg/kg bwt/d
Control Group: other: deionized water
NOAEL: = 1000 mg/kg bw

Method: Directive 84/449/EEC, B.7 "Sub-acute toxicity (oral)"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND MAINTANENCE
- Species and strain: rat, SPF Wistar, outbred (BRL Ltd, Basel, Switzerland)
- Numbers: 20 males, 20 females
- Age: approx. 6 wk at start of treatment
- Acclimation period: at least 5 d
- Housing: group housed (5 per cage) in suspended wire mesh cages
- Diet: Kliba pelleted laboratory animal diet (Klingentalmuehle AG, Switzerland), ad libitum
- Water: tap water, ad libitum
- Environment: controlled to 21 degrees C, 55% rel. humidity, 12 hr light/dark cycle, 15 air changes/hr

PREPARATION OF DOSING SOLUTIONS
The test substance was dosed undiluted.

ANALYSIS OF DOSING SOLUTIONS
None performed.

TREATMENT
Test substance administered by oral gavage to groups of 5 male and 5 female rats at dose levels of 0 (deionized water), 300, 600 or 1000 mg/kg bwt/d for 14 consecutive days. Dose volumes (calculated weekly according to bwt) were 0.99, 0.30, 0.59 or 0.99 ml/kg bwt/day, respectively.

OBSERVATIONS

- clinical signs: at least once daily
- morbidity / mortality: twice daily
- body weight: weekly and on the day preceding necropsy, prior to an overnight fast.
- food intake: weekly
- ophthalmic examination: during final week of treatment

CLINICAL CHEMISTRY, HEMATOLOGY
Blood (retro-orbital sinus, light ether anesthesia) was collected immediately prior to necropsy.

Hematology
- a standard range of endpoints was determined on blood containing either EDTA or citrate as anticoagulant (see entry for 90-day study for list of endpoints).

Clinical chemistry
- a standard range of endpoints was determined on serum (see entry for 90-day study for list of endpoints).

NECROPSY AND HISTOPATHOLOGY
The terminal bwt was recorded and the animals sacrificed by exsanguination (deep ether anesthesia) on day 15, following an overnight fast. Any macroscopic abnormalities were noted. The following organs were weighed, preserved and subject to microscopic examination (H&E staining):
- adrenals
- heart
- kidneys
- liver
- spleen
- stomach (not weighed)
- testes
- all gross lesions (not weighed)

STATISTICAL METHODS
- body weights, food intake, organ weights: Dunnett-test (pooled variance)
- hematology, clinical chemistry: Dunnett -test or Steel-test
- ophthalmic observations: Fisher Exact test

Result: All results are presented by dose level (control, 300 mg/kg bwt, 600 mg/kg bwt, 1000 mg/kg bwt).

There was no mortality, morbidity or clinical signs among the treated groups. The only findings of note were:

CLINICAL CHEMISTRY
- total serum protein (g/l), males only: 61, 60, 60, 57 (P<0.01)
- serum creatinine (umol/l), females only: 78.8, 69.7 (P<0.05), 76.5, 74.7
- serum urea (mmol/l), females only: 9.8, 7.2 (P<0.01), 8.2 (P<0.05), 7.7 (P<0.05)

The study director noted that the lack of consistency between the sexes indicated observations were not of toxicological significance.

NECROPSY
One female (animal 28) from the 300 mg/kg bwt/d group had an enlarged liver (+ 90% (absolute and relative) compared to control mean) and spleen (+ 270% abs. and rel.) with histopathological evidence of a lymphoblastic type of leukemia. In view of the short treatment period, this was considered unrelated to treatment by the study director. One female (animal 33) from the 600 mg/kg bwt/d group had a liver nodule (organ wt unaffected, no histopathological abnormality). This was considered the result of normal biological variation by the study director.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: No adverse effects were present in male and female Wistar rats following gavage administration of MP Diol Glycol at doses of 0, 300, 600 or 1000 mg/kg bwt/d for at least 14 days. The results support a definitive sub-acute NOAEL of 1000 mg/kg bwt/day.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

08-AUG-2003 (36)

Type: Sub-chronic
Species: rat **Sex:** male/female
Strain: Wistar
Route of administration: gavage
Exposure period: 90 d
Frequency of treatment: daily
Doses: 0, 300, 600 or 1000 mg/kg bwt/d
Control Group: other: deionized water
NOAEL: = 1000 mg/kg bw

Method: Directive 87/302/EEC, part B, p. 8 "Sub-chronic oral toxicity test: 90-day repeated oral dose using rodent species"
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND MAINTANENCE
- Species and strain: rat, SPF Wistar, outbred (BRL Ltd, Basel, Switzerland)
- Numbers: 45 males, 45 females

- Distribution to treatment groups: 10/sex/dose level (plus 5 spare per sex)
- Age: approx. 6 wk at start of treatment
- Acclimation period: at least 5 d followed by veterinary health examination
- Housing: group housed (5 per cage) in suspended wire mesh cages
- Diet: Kliba pelleted laboratory animal diet (Klingentalmuehle AG, Switzerland), ad libitum
- Water: tap water, ad libitum
- Environment: controlled to 21 +/- 3 degrees C, 40-70% rel. humidity, 12 hr light/dark cycle, 15 air changes/hr

PREPARATION OF DOSING SOLUTIONS
The test substance was dosed undiluted.

ANALYSIS OF DOSING SOLUTIONS
None performed.

TREATMENT
Test substance administered by oral gavage (metal stomach tube) to groups of 10 male and 10 female rats at dose levels of 0 (deionized water), 300, 600 or 1000 mg/kg bwt/d for at least 91 consecutive days. Dose volumes (calculated weekly according to bwt) were 0.99, 0.30, 0.59 or 0.99 ml/kg bwt/day, respectively.

OBSERVATIONS
- morbidity / mortality: twice daily
- clinical signs: at least once daily on study days 1-28, weekly thereafter
- palpation: each animal handled and subject to physical examination once weekly
- body weight and food intake: weekly
- ophthalmic examination: during final week of treatment (control and 1000 mg/kg bwt/d groups only)

CLINICAL CHEMISTRY, HEMATOLOGY
Blood (retro-orbital sinus, light ether anesthesia) was collected immediately prior to necropsy following an overnight fast.

Hematology
- a standard range of endpoints was determined on blood containing either EDTA or citrate as anticoagulant:
- erythrocyte count
- hemoglobin concentration
- hematocrit
- mean corpuscular hemoglobin
- mean corpuscular hemoglobin concentration
- platelet count
- red cell distribution width
- total leukocyte count- differential white cell count
- prothrombin time

- partial thromboplastin time

Clinical chemistry
- a standard range of endpoints was determined on serum:
- ALAT (GPT), ASAT (GOT), alkaline phosphatase
- bilirubin, creatinine, glucose, urea
- total protein, albumin
- sodium, potassium, chloride, calcium, phosphorus

NECROPSY AND HISTOPATHOLOGY
The terminal bwt was recorded and the animals sacrificed by exsanguination (deep ether anesthesia) on day 15, following an overnight fast. Any macroscopic abnormalities were noted. The following organs were weighed:
- adrenals
- brain
- heart
- kidneys
- liver
- spleen
- testes

Samples were preserved from the following organs:
- adrenals, aorta
- brain
- cecum, cervix, clitoral gland #, colon
- duodenum
- epididymides, esophagus, eyes (+ optic nerve and Harderian gland)
- femur (incl. joint)
- heart
- ileum
- jejunum
- kidneys
- larynx #, lachrymal gland (exorbital) #, liver, lungs (infused with formalin), lymph nodes (mandibular, mesenteric)
- mammary gland
-ovaries
- pancreas, pituitary gland, preputial gland #, prostate gland
- rectum
- salivary glands (mandibular, sublingual), sciatic nerve, seminal vesicles, skeletal muscle, skin, spinal cord (cervical, mid-thoracic, lumbar), spleen, sternum with bone marrow, stomach
- testes, thymus, thyroid (incl. parathyroid), tongue#, trachea
- urinary bladder
- vagina- all gross lesions
Tissues from control and 1000 mg/kg bwt/d groups (and any gross lesions) were subject to histopathological examination (excluding tissues marked #) after wax embedding and H&E staining.

STATISTICAL METHODS
- body weights, food intake, organ weights: Dunnett-test (pooled variance)
- hematology, clinical chemistry: Dunnett -test or Steel-test
- ophthalmic observations: Fisher Exact test

Result: All results are presented by dose level (control, 300 mg/kg bwt, 600 mg/kg bwt, 1000 mg/kg bwt).

There was no mortality, morbidity or clinical signs or changes in behavior among the groups. Results for the majority of endpoints were comparable for control and treated animals, with only minor variations present in most instances.

The only findings of note were:

CLINICAL CHEMISTRY
ALAT(U/l), males only: 0.58, 0.56, 0.62, 0.50 (P<0.05)
ASAT (U/l) males only: 2.06, 2.20, 1.96, 1.82 (P<0.05)
Total bilirubin (umol/l) males only: 2, 2, 3 (P<0.05), 2
Phosphorus (mmol/l), males only: 1.91, 1.72 (P<0.05), 1.75 (P<0.05), 1.71 (P<0.05)
The study director concluded that these changes were either of no biological significance (ALAT, ASAT) or were spontaneous, non-treatment related events (bilirubin, phosphorus).

NECROPSY
Liver wt, males:
- absolute (g): 12.49, 11.63, 11.42, 12.78 (non-sig.)
- relative (g/100 g bwt): 3.19, 2.90 (P<0.05), 2.84 (P<0.01), 3.14
Liver wt, females:
- absolute (g): 8.60, 7.51 (P<0.01), 7.64 (P<0.01), 8.45
- relative (g/100 g bwt): 3.50, 3.16 (P<0.01), 3.15 (P<0.01), 3.36
Kidney wt, females
- absolute (g): 1.56, 1.59, 1.60, 1.71 (P<0.05)
- relative (g/100 g bwt): 0.63, 0.67, 0.66, 0.68 (non-sig.)
Since these alterations were not expressed consistently (within a sex or between sexes) and no dose/response relationship was present, the study director concluded they were unrelated to administration of MP Diol Glycol.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: No adverse effects were present in male and female Wistar rats following gavage administration of MP Diol Glycol at

doses of 0, 300, 600 or 1000 mg/kg bwt/d for at least 90 days. The results support a definitive sub-chronic NOAEL of 1000 mg/kg bwt/day.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

08-AUG-2003 (35)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA1537, TA98, TA1535, TA100
Concentration: 100-5000 ug/plate
Cytotoxic Concentration: >5000 ug/plate
Metabolic activation: with and without
Result: negative

Method: Directive 84/449/EEC, B.14
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: DIRECT PLATE INCORPORATION ASSAY
Five dose levels (spaced at approx. half-log intervals) were tested in triplicate in each strain. The test was conducted twice, in the presence and absence of S9 on both occasions. The test system contained:
- top agar (3 ml)
- bacterial culture (10^9 cells/ml; 0.1 ml)
- test substance in sterile reverse osmosis (Milli-Q) water
- S9 mix (activation assays; 0.5 ml) or 0.1 M phosphate buffer, pH 7.4 (non-activation assays; 0.5 ml)

COLONY COUNTING
His+ revertants were counted using an Artek 880 colony counter, or by manual counting if <40 colonies present.

S9 MIX (per 10 ml)
- NADP (30 mg) and glucose-6-phosphate (15.2 mg; in total volume 5.5 ml water)
- sodium phosphate buffer (0.5 M, pH 7.4, 2 ml)
- magnesium chloride (0.08 M, 1 ml)
- potassium chloride (0.33 M, 1 ml)
- Arochlor 1254-induced rat liver S9: 0.5 ml

SELECTION OF DOSE LEVELS
A preliminary toxicity test was performed using TA100 and concentrations of MP Diol Glycol (1-5000 ug/plate, in duplicate), with and without S9. The preliminary test was also used to assess cytotoxicity.

The main assays were performed using 100, 333, 1000, 3330

and 5000 ug/plate.

Negative control: vehicle (sterile, reverse osmosis water)

Positive controls: without S9
- TA1535: sodium azide (1 ug/plate)
- TA1537: 9-aminoacridine (60 ug/plate)
- TA98: daunomycine (4 ug/plate)
- TA100: methylmethanesulfonate (650 ug/plate)

Positive controls: with S9
- TA1535 and TA 1537: 2-aminoanthracene (5 ug/plate)
- TA98 and TA100: 2-aminoanthracene (0.5 ug/plate)

ACCEPTABILITY CRITERIA
- spontaneous reversion data (negative controls) within historical range for laboratory
- response of positive control substances within historical range for laboratory
- dose range used for test substance should exhibit clear evidence of cytotoxicity or should extend to 5000 ug/plate

EVALUATION CRITERIA
A result was considered negative if:
- number of revertants <2-fold that of solvent control (both with and without S9 activation)
- negative response was reproducible in both independent assays

A results was considered positive if:
- number of revertants >2-fold that of solvent control (both with and without S9 activation), disregarding plates with 20 colonies or less
- positive response was reproducible in both independent assays

No statistical analyses were carried out.

Result: CYTOTOXICITY
Survival of TA100 in the preliminary test (and all tester strains from the main study) was unaffected by MP Diol Glycol at 5000 ug/plate both in the presence and absence of S9.

RESULTS FROM MAIN TRIALS
A negative response was obtained in all tester strains over the entire range of concentrations tested in both trials, in the presence and absence of S9.

RESULTS FOR CONTROLS
A satisfactory response was obtained with the negative and positive control plates.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA

Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: MP Diol Glycol was not mutagenic in Salmonella typhimurium TA 1535, TA 1537, TA98 or TA100 when tested with independent repeat at 100-5000 ug/plate in the presence and absence of Arochlor 1254-induced rat liver S9.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

24-JUL-2003 (41)

Type: Chromosomal aberration test
System of testing: Human lymphocytes
Concentration: 10-5000 ug/ml without S9; 333-5000 ug/ml with S9
Cytotoxic Concentration: >5000 ug/l
Metabolic activation: with and without
Result: negative

Method: Directive 84/449/EEC, B.10
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
Cultured peripheral human lymphocytes were established within 4 hr of taking blood from three adult male donors.

CELL CULTURE CONDITIONS
Whole blood (0.4 ml) was cultured for 48 hr in F10 complete culture medium (5 ml) with phytohemagglutinin (0.1 ml) prior to use. Incubations were performed in the dark in humidified (80-95%) air containing 5% carbon dioxide. Temperature, humidity and CO2 levels were monitored during the experiment.

EXPERIMENTAL DETAILS
The test system contained:
- lymphocyte culture (0.4 ml blood in 5 ml medium)
- test substance in sterile reverse osmosis (Milli-Q) water (volume not given)
- S9 mix (activation assays; 0.2 ml) or HEPES (non-activation assays; 0.2 ml)

Test in the presence of S9: after 3 hr treatment, cells were rinsed (HBSS) for a further 20-22 hr (first fixation period) or 44-46 hr (second fixation period).

Test in the absence of S9: cells were fixed immediately after treatment for 24 hr and 48 hr.

Colchicine (0.5 ug/ml) was added to arrest cell division during the last 3 hr of culture. Thereafter the cells were

treated with hypotonic potassium chloride (0.56%) and fixed with methanol. Two slides per culture were stained with Giemsa and embedded in DePeX.

S9 MIX (per 1 ml)
- NADP (3.4 mg)
- glucose-6-phosphate (1.7 mg)
- HEPES (4 umol)
- MgCl2.6H20 (1.02 mg)
- KCl (2.46 mg)
- Arochlor 1254-induced rat liver S9: 0.5 ml

SELECTION OF DOSE LEVELS
A preliminary toxicity test (10, 33, 100, 333, 1000, 3330 and 5000 ug/ml) was performed to determine if MP Diol Glycol inhibited mitosis in the presence or absence of S9 mix. Mitotic index in the 5000 ug/ml cultures in the absence of S9 was reduced by 37% after the first fixation period and by 47% after the second. In the presence of S9 after 24 hr fixation the mitotic index was reduced by 24% at 5000 ug/ml. As a result, the following treatment levels were selected for the main experiments:
Experiment 1
- S9: 10, 100, 1000 and 5000 ug/plate
+ S9: 333, 1000, 3330 and 5000 ug/plate
Experiment 2
- S9: 333, 1000, 3330 and 5000 ug/plate
+ S9: 333, 1000, 3330 and 5000 ug/plate

CONTROL SUBSTANCES
Negative control: F10 medium buffered with 20 mM HEPES

Positive control: without S9
Mitomycin C (0.2 ug/ml for 24 hr; 0.1 ug/ml for 48 hr)

Positive control: with S9
Cyclophosphamide (15 ug/ml for 3 hr)

MITOTIC INDEX
The mitotic index of each culture was determined by counting the number of metaphases per 1000 cells.

CHROMOSOMAL ABERRATIONS
Slides were randomly coded and scored 'blind'. At least 100 metaphase chromosome spreads per culture were examined (metaphases with <46 chromosomes excluded from analysis). The number of cells with aberrations and the number of aberrations were calculated.

ACCEPTABILITY CRITERIA
The test was considered acceptable if it met the following criteria:
- chromosomal aberrations in the solvent control cultures should fall within the laboratory historical range;

- the positive control substances should give a significant (P<0.05; Chi-square test) increase in cells with chromosomal aberrations.

EVALUATION CRITERIA
A result was considered negative if:
- none of the tested concentrations induced a statistically significant (P<0.05; Chi-square test) increase in cells with chromosomal aberrations;

A result was considered positive if:
- there was a dose-related, statistically significant (P<0.05; Chi-square test) increase in cells with chromosomal aberrations;
- no dose-response was observed but a statistically significant (P<0.05; Chi-square test) increase in chromosomal aberrations was present in both independent repeat tests.

STATISTICAL METHODS
The Chi-square test was used to compare results from each treatment group with the controls.

Result: Results from the preliminary study demonstrated that pH and osmolarity were unaffected by inclusion of 5000 ug/ml MP Diol Glycol in the cultures (7.81 and 291 mOsm/kg respectively for control, 7.88 and 344 mOsm/kg respectively in presence of test substance).

There was no statistically significant or biologically meaningful increase in chromosomal aberrations (excluding gaps) in either experiment in the absence or presence of S9 e.g.
Experiment 1, 5000 ug/ml:
-S9, 24 hr fixation: 1-2 aberrant cells per 100 metaphases
-S9, 48 hr fixation: 0-1
+S9, 24 hr fixation: 0-0
+S9, 48 hr fixation: 0-1
Experiment 2, 5000 ug/ml:
-S9, 24 hr fixation: 0-0 (no 48 hr evaluation)
+S9, 24 hr fixation: 0-1 (no 48 hr evaluation)

The number of cells with chromosomal aberrations (excluding gaps) in the solvent control cultures was within the historical control range (1.1 +/- 1.0 aberrant cells per 100 metaphases -S9; 1.1 +/- 0.8 aberrant cells per 100 metaphases +S9).

A satisfactory response was obtained with the positive control substances.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A

Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: MP Diol Glycol was not clastogenic in human peripheral lymphocytes when tested at concentrations up to 5000 ug/ml in the presence and absence of Arochlor 1254-induced rat liver S9.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

24-JUL-2003 (39)

Type: Mammalian cell gene mutation assay
System of testing: V79 Chinese hamster cells

Method: Directive 2000/32/EC, B.17
Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: TEST SYSTEM
V79 Chinese hamster cells were obtained from the Department of Toxicology, Agricultural College of Wageningen, the Netherlands.

CELL CULTURE CONDITIONS
V79 cells were cultured at 37 degrees C in F10 complete culture medium in humidified air (80-95%) containing 5% carbon dioxide. Temperature and CO2 levels were monitored during the experiment. Prior to mutagenicity testing, cells were grown for 4-5 days on culture medium containing hypoxanthine 10^-4 M), aminopterin (10^-5 M) and thymidine (1.6 x 10^-5 M) to reduce occurrence of spontaneous mutations.

EXPERIMENTAL DETAILS
Cells were exposed to the test substance in F10 complete culture medium without serum, buffered with 20 mM HEPES, for 3 hr. The test system contained:
- V79 cells (6 x 10^16 in 6 ml medium)
- test substance (F10 medium buffered with 20 mM HEPES)
- S9 mix (activation assays; 0.2 ml) or HEPES (non-activation assays; 0.2 ml)

After exposure, the cells were rinsed twice with Hank's balanced salt solution, resuspended in complete culture medium, counted and seeded for determination of colony forming efficiency and for expression of mutant phenotype. The cells were subcultured twice during the 7 day expression period. Colony forming efficiency was assessed by plating 200 cells in triplicate. Mutant frequency was assessed by seeding 10^6 cells into petri dishes containing 10 ml selective medium, and incubating for 7-10 days. Colony counts were performed using an Artek colony counter.

S9 MIX (per 1 ml)
- NADP (3.4 mg)
- glucose-6-phosphate (1.7 mg)
- HEPES (4 umol)
- MgCl2.6H20 (1.02 mg)
- KCl (2.46 mg)
- Arochlor 1254-induced rat liver S9: 0.5 ml

SELECTION OF DOSE LEVELS
A preliminary toxicity test was performed in the presence or absence of S9 mix to determine if MP Diol Glycol (10, 33, 100, 333, 1000, 3330 and 5000 ug/ml) was toxic toward V79 cells. Cytotoxicity was expressed as the reduction in colony forming efficiency compared to the solvent control. No adverse effect was apparent, hence the following exposure range was used in the main studies (with and without S9): 333, 1000, 3330 and 5000 ug/ml

CONTROL SUBSTANCES
Negative control: F10 medium buffered with 20 mM HEPES

Positive control: without S9
Ethylmethanesulfonate (6 mM in DMSO)

Positive control: with S9
Dimethylnitrosamine (8 mM in HBSS)

ACCEPTABILITY CRITERIA
The test was considered acceptable if it met the following criteria:
- absolute cloning efficiency equal to or greater than 50%;
- acceptable number of surviving cells in at least 3 of the 4 doses tested
- spontaneous mutation frequency in untreated or solvent controls <5 x 10^5 survivors;
- significant (at least 3-fold) response in mutant frequency for positive controls.

EVALUATION CRITERIA
A result was considered negative if:
- none of the tested concentrations showed a mutant frequency at least 3-fold that of the solvent control;
- the result was confirmed in an independent test.

A results was considered positive if:
- the test substance produced a mutant frequency 3-fold higher than the spontaneous mutation frequency of the solvent controls;
- a dose response relationship was present and reproducible in an independently repeated test.

STATISTICAL METHODS
No statistical methods were applied to the data.

Result: Results from the preliminary study demonstrated that cloning

efficiency directly after exposure to 333-5000 ug MP Diol Glycol/ml medium was decreased by approx. 25-40% (no clear concentration response/relationship; similar response in absence or presence of S9). pH and osmolarity were unaffected by inclusion of 5000 ug/ml MP Diol Glycol in the cultures (7.47 and 298 mOsm/kg respectively for control, 7.42 and 344 mOsm/kg respectively in presence of test substance).

There was no increase in mutant frequency at the HPRT-locus in either of the independent repeat studies. A satisfactory response was obtained for both the solvent control and positive control substances.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: MP Diol Glycol was not mutagenic in the V79/HPRT mutation test system when tested at concentrations up to 5000 ug/ml in the presence and absence of Arochlor 1254-induced rat liver S9.

Reliability: (1) valid without restriction
Report available for review. GLP-compliant guideline study.

30-JUN-2003 (40)

5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8.1 Toxicity to Fertility

Type: Two generation study
Species: rat
Sex: male/female
Strain: Sprague-Dawley
Route of administration: gavage
Exposure Period: at least 70 d prior to mating
Frequency of treatment: daily
Doses: 0, 100, 300 or 1000 mg/kg bwt/d
Control Group: other: yes (deionized water)
NOAEL Parental: = 1000 mg/kg bw
NOAEL F1 Offspring: = 1000 mg/kg bw
NOAEL F2 Offspring: = 1000 mg/kg bw

Method: EPA OPPTS 870.3800
Year: 2000
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND MAINTANENCE
- Species and strain: rat, Crl:CD (SD)IGS BR (Charles River Laboratories, Raleigh, NC, USA)
- Age: 29 days on receipt
- Acclimation period: 15 d
- Housing: individually housed in suspended wire mesh cages
- Diet: Certified Rodent Lab Diet 5002 (PMI Nutrition International Inc.), ad libitum
- Water: reverse osmosis-treated tap water, ad libitum
- Environment: controlled to 72 +/- 4 degrees F, 30-70% rel. humidity, 12 hr light/dark cycle, 10 air changes/hr
- F0 age at first treatment: approx. 6 wk
- F0 bwt at first treatment: males = 186-264g, females 141-184g

PREPARATION OF DOSING SOLUTIONS
Dosing solutions were prepared biweekly in deionized water vehicle to give target concentrations of 0, 20, 60 or 200 mg/ml, and stored at room temperature.

ANALYSIS OF DOSING SOLUTIONS
An aliquot (from the middle stratum of each formulation) was taken from each bi-weekly preparation and analyzed by GC. Stability was determined over 17 days (room temperature).

TREATMENT
Test substance administered by oral gavage (stainless steel cannula; 5 ml/kg bwt) at dose levels of 0 (deionized water), 100, 300 or 1000 mg/kg bwt/d to F0 males and females for a minimum of 70 days prior to mating. Doses were based upon the most recently recorded individual body weight data. Dosing continued throughout mating, gestation and lactation until euthanasia. The F1 generation was exposed in utero, through nursing, during lactation and through weaning. F1

males and females selected for mating were treated from PND 22 as described for the F0 generation.

MATING
Animals (30 per sex per dose group, both F0 and F1 generations) were paired in a 1:1 basis after treatment for at least 70 d. Each pair was examined daily and mating was confirmed by the presence of a copulatory plug or presence of sperm in a vaginal smear (assigned GD 0). If no evidence of mating was apparent after 14 d (or three estrus cycles), the female was placed in a plastic maternity cage with nesting material.F0 bwt prior to mating (wk 10; age approx. 12 wk): males 437-682 g, females 202-367 gF1 bwt prior to mating (wk 28; age approx. 15 wk): males 415-636 g, females 225-368 g

F0 AND F1 OBSERVATIONS
All animals observed three times per day for external clinical signs, behavioral changes and mortality, and subject to a more detailed physical examination once weekly. Male body weight and food intake were recorded weekly until euthanasia. Female body weight and food consumption were recorded weekly until mating, on 6 occasions during gestation (3-6 d intervals) and regularly during lactation (3-7 d intervals). The stage of estrus (metestrus, diestrus, estrus, proestrus) for each female (vaginal smear) was recorded commencing from 21 d prior to mating and continuing until mating was confirmed.

LITTER OBSERVATIONS
Each litter was examined daily for survival. Any pups dying on PND 0-4 were subject to necropsy (including examination of heart and brain plus skeletal examination if hard tissue anomaly suspected). A detailed gross necropsy was conducted on any pup dying between PND 4 and prior to weaning, and tissues preserved for histological examination.

LITTER REDUCTION
Litter size was reduced to 8 pups per litter (4 male, 4 female as far as possible) to reduce variability among litters.

PUP PARAMETERS
Each pup was subject to a detailed physical examination on PND 1, 4, 7, 14 and 21. Anogential distance was measured on PND1, and pups individually sexed on PND 0, 4 and 21. Body weights were recorded on PND 1, 4, 7, 14 and 21.

DEVELOPMENTAL LANDMARKS
Balanopreputial separation was assessed in males (n = 30 per dose group) from PND 35 onwards. Vaginal opening was assessed in females (n = 35 per dose group) from PND 25 onwards. Body weight was recorded for all pups on the day of acquisition of each developmental landmark.

SELECTION OF F1 PARENTS
35 male and 35 female F1 pups were randomly selected from each dose group on PND 21 (weaning), and treated (control or MP Diol) on PND 22-27. 30 animals per sex per dose group were selected to comprise the F1 generation, the remaining animals were subject to post-mortem examination (emphasis on developmental morphology).

NECROPSY - ADULTS
All F0 and F1 parental animals were subject to examination (including any unscheduled deaths). Organ weights were recorded for all major organs, including epididymides (total and cauda), ovaries, prostate, seminal vesicles (with coagulating glands and accessory fluids), testes and uterus with oviducts and cervix. An extensive range of tissues (in excess of 30 organs/organ systems plus any abnormal tissues) were sampled and preserved.

EVALUATION OF SPERMATOGENIC ENDPOINTS
The right epididymis was excised immediately upon euthanization, weighed and a sample of sperm collected from the right cauda epididymis for assessment of:
- motility (200 motile and nonmotile spermatozoa per animal, all dose groups, Hamiliton-Thorne HTM-IVOS Version 10 computer assisted sperm analysis system)
- morphology of abnormal forms evaluated by differential microscopic count of 22 spermatozoa per animal light using wet-mount technique (Linder et al. (1992) Reprod Toxicol., 6, 491-505)
- left testis and epididymis from all males stored frozen, homogenized and assessed for homogenization resistant sperm and sperm production rates (minimum of 200 cells if possible or 20 fields counted per sample; method of Blazak et al. (1985), Fund Appl Toxicol, 5, 1097-1103)

NECROPSY - PUPS
5 'selected' F1 pups/sex/group (see "Selection of F1 parents) were subject for post-mortem examination on PND28. All other 'unselected' F1 pups and all F2 weanlings were subject to post-mortem examination of PND 21. Brain, spleen and thymus weights were recorded for one randomly selected male and female per litter. All gross lesions were retained, all other tissues discarded.

HISTOPATHOLOGY
Microscopic evaluation of the following tissues was performed on F0 and F1 animals (10 per sex per dose group) from the control and high dose groups:
adrenal glands, brain, cervix, coagulating gland, epididymides (right), kidneys, liver, ovaries, oviducts, pituitary, prostate, seminal vesicles, spleen, testis (right), thymus, uterus, vagina, vas deferens and all gross lesions (from all dose groups).

STATISTICAL METHODS
- mating and fertility indices: Chi-square test with Yates correction
- sperm motility, morphology, postnatal survival: Kruskal-Wallis test with Mann-Whitney U test
- histopathology findings: Kolmogorov-Smirnov test
- all other continuous data: One-way ANOVA with Dunnett's test

Result:

ANALYSIS OF DOSING SOLUTIONS
Results of periodic concentration analyses (n=19/dose level) returned the following mean concentrations:

-----mg/ml-----		
Target	Actual	SD
20	19.7	0.98
60	59.7	2.48
200	198	7.70

All results are presented by dose level (control, 100 mg/kg bwt, 300 mg/kg bwt, 1000 mg/kg bwt).

CLINICAL OBSERVATIONS AND SURVIVAL
No test substance-related clinical findings were apparent. One male (No. 14870) from the 300 mg/kg bwt/day F0 generation group was euthanized in extremis during study week 2 with pyelonephritis, all other F0 and F1 parental animals survived to scheduled necropsy.

REPRODUCTIVE PERFORMANCE
MP Diol did not adversely affect reproductive performance in either sex from F0 or F1 generations.

Mating index
- F0: 93.3%, 96.7%, 100.0%, 100.0%
- F1: 100.0%, 90.0%, 100.0%, 96.7%

Fertility index
- F0: 80.0%, 96.7%, 100.0% (P<0.05; increased), 93.3%
- F1: 89.7%, 80.0%, 93.3%, 93.3%

Mean pre-coital interval (days)
- F0: 2.6, 2.7, 3.0, 3.1
- F1: 2.7, 2.4, 3.5, 2.4

Estrus cycle length (days)
- F0: 4.2, 4.3, 4.1, 4.1
- F1: 4.3, 4.2, 4.9, 4.4

BODY WEIGHT AND FOOD INTAKE
Occasional differences were present in the F0 and F1 parental generations relative to the controls, but these were not considered indicative of an adverse effect by the study director since they were sporadic, small in magnitude (with both increases and decreases in a parameter) and did not exhibit any dose/response relationship.

GESTATION LENGTH
The mean length of gestation was unaffected by treatment in

both generations.
F0: 22.0, 22.1, 22.0, 21.9 days
F1: 21.8, 21.8, 21.8, 22.0 days

SPERMATOGENIC EVALUATIONS
Mean testicular and epididymal sperm numbers, sperm production rate, sperm motility and morphology were comparable between control and treated males from both F0 and F1 generations, with no statistically significant differences present.

NECROPSY OBSERVATIONS
Macroscopic and histological changes in animal no. 14870 from the 300 mg/kg bwt/day F0 generation (sacrificed in extremis during week 2) were consistent with pyelonephritis. Other treated F0 and F1 parental animals were unremarkable.

Macroscopic findings.
There were no treatment-related macroscopic findings.

The mean number of implantation sites did not differ between the groups:
- F0: 15.7, 15.7, 15.8, 16.2
- F1: 14.0, 13.8, 15.5, 15.3

Organ weights
F0 generation parents
300 mg/kg bwt/day
- absolute and relative ovary (both approx. 14%) and adrenal weights (both approx. 9%) increased significantly in females.
1000 mg/kg bwt/day
- absolute and relative ovary (both approx. 18%) and adrenal (both approx. 10%) weights, together with absolute kidney weights (6%), increased significantly in females.

There were no morphological / histological alterations accompanying these changes in organ weights, which were considered unrelated to treatment by the study director. Organ weights in males were unaffected.

F1 generation parents
100 mg/kg bwt/d
- significant increase in absolute weight of left epididymis (7%), and left and right cauda epididymides (approx. 12%) in males; absolute kidney weight increased (6%) in females;
300 mg/kg/d
- significant increase in absolute weight of seminal vesicle and coagulating gland (18%), right and left testis weights (approx. 5%), right and left epididymis and cauda epididymides (18%, 12%) in males;
1000 mg/kg/d
- significant increase in absolute weight of right testis (8%), left epididymis (10%) and right cauda epididymis (13%)

in males; absolute kidney weight increased (6%) in females

Except for a 13% increase in relative right cauda epididymis weight for the 300 mg/kg bwt/day males, none of the above changes were statistically significant when expressed relative to body weight. There were no morphological / histological alterations accompanying these changes in organ weights, which were considered unrelated to treatment by the study director.

Microscopic examination
One male (14870) from the F0 parental 300 mg/kg bwt/day group, sacrificed in extremis during week 2, exhibited changes consistent with pyelonephritis. One female (15042) from the F0 parental 1000 mg/kg bwt/day group had a mammary gland adenocarcinoma. The appearance of all other tissues examined from high dose males and females, including the gonads and accessory systems, were unremarkable.

LITTER DATA
No statistically significant differences were present in litter parameters.

Live litter size:
- F0: 14.5, 14.5, 15.0, 15.1
- F1: 12.9, 12.9, 14.3, 13.4

No. live pups:
- F0: 15.0, 14.9, 15.2, 15.3
- F1: 13.2, 13.0, 14.6, 14.1

Males/litter (%):
- F0: 49.2, 49.9, 49.3, 50.9
- F1: 48.6, 47.1, 49.9, 49.2

PUP SURVIVAL
Pup survival (% alive) was unaffected by treatment:
From birth to PND 4 (pre-selection):
- F1: 91.3, 95.6, 97.2, 96.8
- F2: 95.2, 97.3, 95.1, 90.6

From PND 4 (post-selection) to PND 21:
- F1: 100, 99.6, 100, 99.6
- F2: 99.5, 100.0, 98.7, 99.1

Pup body weight:
Body weight and body weight gain were increased at some time points in some treated litters in both generations, however there was no apparent temporal or dose related trend, and the study director concluded these were unrelated to administration of the test substance.

ANOGENITAL DISTANCE (F1)
There were no significant difference in anogenital distance for F1 pups, however a slight (5-7%) increase was recorded in 300 and 1000 mg/kg bwt/day males from the F2 generation.

These differences were considered slight and of no biological relevance by the study director.
F1 pups
- males (mm): 5.3, 5.2, 5.3, 5.3
- males (relative to cube root of bwt): 2.78, 2.72, 2.77, 2.80
- females (mm): 3.2, 3.1, 3.1, 3.2
- females (relative to cube root of bwt): 1.71, 1.67, 1.65, 1.70
F2 pups
- males (mm): 5.7, 6.0, 6.1 (P<0.05), 6.1 (P<0.05)
- males (relative to cube root of bwt): 3.04, 3.11, 3.18 (P<0.05), 3.20 (P<0.01)
- females (mm): 3.9, 3.9, 4.0, 4.1
- females (relative to cube root of bwt): 2.13, 2.08, 2.14, 2.21

NECROPSY FINDINGS
No treatment-related changes were apparent in either F1 or F2 pups.

DEVELOPMENTAL LANDMARKS (F1)
Balanopreputial separation in the F1 generation was unaffected by treatment (not assessed in F2):
- age of acquisition (days): 44.6, 43.7, 43.4, 43.0
All male pups had balanopreputial separation by PND 53.

Vaginal patency in the F1 generation was unaffected by treatment in any of the pups (not assessed in F2):
- age of acquisition (days): 34.4, 33.8, 34.2, 34.5
All female pups had vaginal opening by PND 40.

There was no statistically significant difference in body weight for acquisition of either landmark.

Test substance: Source: Lyondell Chemical Worldwide Inc, Newtown Square, PA, USA.
Identity: MP Diol Glycol
Lot ACX 81019-1846; supplied in 3 batches (November 1998, February 1999, September 1999)
Purity: 98.67% by weight.
Expiration date: not reported

Conclusion: No parental, neonatal or reproductive toxicity was observed following administration of MP Diol at dose levels of 100, 300 or 1000 mg/kg bwt/day over two generations. The NOAEL for parental, neonatal and reproductive effects was therefore 1000 mg/kg bwt/day.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

26-NOV-2003 (33)

Type: other: effects on gonads after sub-chronic oral exposure
Species: rat
Sex: male/female
Strain: Wistar
Route of administration: gavage
Exposure Period: 90 d
Frequency of treatment: daily
Doses: 0, 300, 600 or 1000 mg/kg bwt/d
Control Group: other: deionized water
NOAEL Parental: = 1000 mg/kg bw

Year: 1993
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Remark: See entry for sub-chronic toxicity study for further details:

ANIMALS AND MAINTANENCE
- Species and strain: rat, SPF Wistar, outbred (BRL Ltd, Basel, Switzerland)
- Distribution to treatment groups: 10/sex/dose level (plus 5 spare per sex)

TREATMENT
Test substance administered by oral gavage (metal stomach tune) to groups of 10 male and 10 female rats at dose levels of 0 (deionized water), 300, 600 or 1000 mg/kg bwt/d for at least 91 consecutive days.

NECROPSY AND HISTOPATHOLOGY
Testis weight were recorded at necropsy.
Samples of the following organs were preserved:
- cervix
- epididymides
- mammary gland
- ovaries
- prostate gland
- seminal vesicles
- testes
- vagina

Tissue from control and 1000 mg/kg bwt/d groups were subject to histopathological evaluation after wax embedding and H&E staining.

Test substance: Identification: MP Diol Glycol
CAS No: 2163-42-0
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: 20609-A
Purity: 99%
Storage conditions: Room temperature, tightly closed container in the dark

Conclusion: There was no evidence of microscopic lesions in the

reproductive system of male or female Wistar rats following sub-chronic gavage administration of MP Diol Glycol at a dose of 1000 mg/kg bwt/d for at least 90 days. The results support a definitive sub-chronic NOAEL 1000 mg/kg bwt/day for microscopic reproductive lesions of the reproductive system in male and female rats.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

30-JUN-2003 (35)

5.8.2 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain: Wistar
Route of administration: gavage
Exposure period: GD 0-20
Frequency of treatment: daily
Doses: 0, 300, 600 or 1000 mg/kg bwt/d
Control Group: other: yes (sterile water)
NOAEL Maternal Toxity: = 1000 mg/kg bw
NOAEL Teratogenicity: = 1000 mg/kg bw
NOAEL Embryotoxicity : = 1000 mg/kg bw

Method: Directive 87/302/EEC, part B, p. 24 "Teratogenicity test - rodent and non-rodent"
Year: 1998
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND MAINTANENCE
- Species and strain: rat, Wistar, Crl: (WI) BR (outbred, SPF quality; Charles River, Sulzfeld, Germany)
- Females: nulliparous and non-pregnant at initiation of study, 11 day acclimation period, n = 120, bwt = 223-294 g- Males: stock animals (no further details)
- Housing: pregnant females individually housed (plastic cages) with purified sawdust for bedding. Dose groups/cages randomly arranged (latin square design) during gestation.
- Diet: standard pelleted diet (Carfil Quality BVBA, Belgium), ad libitum- Water: tap water, ad libitum
- Environment: controlled to 22 +/1 3 degrees C, 30-70% rel. humidity, 12 hr light/dark cycle, 15 air changes per hour

MATING
One female was placed with one resident breeding male (n = 120 per sex) and checked each morning for evidence of mating (vaginal plug, presence of spermatozoa in vaginal smear). The animals were separated once mating was confirmed, and mating discontinued when a total of 96 pregnancies were confirmed. Pregnant females were randomly allocated to treatment groups (n = 24/dose level). The day of mating was

designated GD 0.

TREATMENT
Test substance administered undiluted by oral gavage (rubber stomach catheter) once daily on GD 0-20 to groups of 24 females at dose levels of 0 (milli-U water), 300, 600 or 1000 mg/kg bwt/day. The dosing volume was 0.99, 0.30, 0.59 or 0.99 ml/kg bwt/day.

MATERNAL OBSERVATIONS
Dams were observed at least once daily for clinical signs, including evidence of abortion or premature birth. Body weight was recorded daily on GD 0-21, inclusive. Food intake was recorded on GD 0-3, 3-6, 6-9, 9-13, 13-17 and 17-21.

NECROPSY
Dams were subject to a post-mortem examination of GD 21 (euthanized with carbon dioxide and dislocation of the cervical vertebrae). External surfaces and the interior of the body cavity were examined for macroscopic abnormalities. The ovaries and uterine horns were removed as quickly as possible, and examined for:
- number of corpora lutea (ovaries in situ)- weight of gravid uterus
- number, location, weight and sex of live fetuses- number and location of embryo-fetal deaths
- externally visible (macroscopic) fetal abnormalities

Embryo-fetal deaths were classified as:
- embryonic resorption: only placenta visible at necropsy
- fetal resorption: both placental and embryonic/fetal remains present

Late deaths (dead fetuses showing no resorption) were recorded separately.

The ovaries and genital tract were excised and preserved in buffered formalin, but not processed further.

FETAL DATA
All fetuses were examined externally, euthanized with carbon dioxide and alternate live fetuses preserved either in 96% ethanol (for subsequent possible evisceration and staining with alizarin red S for skeletal examination; no further details) or using Bouin's fluid (for possible detailed visceral examination after free-hand sectioning using a modified Wilson technique). Only fetuses from the control and 1000 mg/kg bwt/day groups were subject to fetal examination, which was conducted by Tesh Consultants International (Suffolk, UK)

REPRODUCTION DATA
Data were collected to assess the following endpoints:
- pre-implantation loss

- implantation index
- post-implantation loss
- implantation site scar index
- embryonic/fetal death index
- embryonic resorption index
- fetal resorption index
- total, live and dead fetus index
- abnormal fetus index
- percentage males and percentage females (total + live)
- mean weight (total plus per sex)

STATISTICAL METHODS
Body weights, food intake: Dunnett-test (pooled variance)
Litter size, implantation data, fetal numbers, fetal loss: Mann-Whitney test
Reproduction data, fetal numbers: Fisher's Exact test or Steel test

Result: Results from this study have been reviewed by Irvine (1999), who made the following additional observations:

- The percentage of embryo-fetal deaths reported for the 600 and 1000 mg/kg bwt/day groups (6.0% and 6.6%, respectively) appeared to have been skewed by unusually high incidences of embryonic deaths in a single female in each group;

- In the high dose group, one female had an exceptionally high number of implantations (22), and the higher incidence of embryonic deaths (9) had the effect of reducing the live litter size to a more normal number (13);

- At the time this study was conducted, the laboratory (NOTOX) had only completed one preliminary and three main OECD 414 studies using rats of this strain; a further two main studies were conducted within the following 4 months, increasing the amount of background information available (135 control dams). This confirmed the view of the study director that the findings in the MP Diol Glycol treated group were within the historical background range for the laboratory;

- Information on pregnancy parameters obtained from the supplier showed that the mean number of embryo-fetal deaths in controls from NOTOX study 213536 (1.5% per group) was markedly lower than expected (range 5.1-21.2%; based on 275 pregnancies). Indeed, results obtained from dams given MP Diol Glycol (means in range 4.0-6.6%) were more representative of the expected number of embryo-fetal deaths than were results from the contemporaneous controls.

Reference: Irvine, L (1999) MP Diol Glycol: Review of NOTOX embryotoxicity study report (213536). Unpublished report, TAS-Environ, Worcs, UK, for Lyondell Chemical Company, PA, USA.

All results are presented by dose level (control, 300 mg/kg bwt, 600 mg/kg bwt, 1000 mg/kg bwt)

MATERNAL EFFECTS
There was no morbidity or premature deaths among the control or treated females. No clinical signs were present at any dose level. (Alopecia was present in a few dams from all dose groups, but no dose relationship was apparent in its incidence or severity.)

There were no statistically significant differences in body weight, body weight gain or food intake between the groups. Corrected maternal body weight gain (i.e. body weight gain on GD0 to GD21 minus gravid uterus weight) was comparable in all groups:
- 57.6 g, 58.1 g, 59.0 g, 62.4 g

No macroscopic abnormalities were present at necropsy.

MATERNAL REPRODUCTION DATA
With the exception of a single female from the 1000 mg/kg bwt/day group, all females were pregnant. There were no differences in pre-implantation loss. There was no statistically significant difference in the number of live fetuses.

Total post-implantation losses, embryonic/fetal deaths and embryonic resorptions were increased significantly in litters from dams given 300 or 1000 mg MP Diol /kg bwt/day:
Post-implantation loss (% of implantation sites):
- per group: 1.8, 4.0, 6.0 (P<0.01), 6.6 (P<0.01)
- per litter: 1.9, 4.3, 6.1 (P<0.05), 6.1 (P<0.05)
Total embryonic/fetal deaths (% of implantation sites):
- per group: 1.5, 4.0 (P<0.05), 6.0 (P<0.01), 6.6 (P<0.01)
- per litter: 1.6, 4.3, 6.1 (P<0.05), 6.1 (P<0.01)
Embryonic resorptions (% of implantation sites):
- per group: 1.5, 3.7 (P<0.05), 6.0 (P<0.01), 6.4 (P<0.01)
- per litter: 1.6, 4.0, 6.1 (P<0.05), 5.9 (P<0.05)

Reviewer's comment: although reported as three separate endpoints, it is evident that the preceding calculations were based on a common dataset that was strongly influenced by the number of embryonic losses (6, 14, 23, 24) observed. This explains in large part the numerical consistency of the three endpoints.

Historical control data (based on litters from 117 females), included the report, suggest that the concurrent control data were at the lower end of the historic range i.e.
- Post-implantation loss (%): mean = 3.1, SD = 2.6, 95% CI = 0.4-5.8
- Total embryonic/fetal deaths (%): mean = 2.8, SD = 2.5, 95% CI = 0.1-5.4
- Embryonic resorptions (%): mean = 2.8, SD = 2.5, 95% CI =

0.1-5.4

Historical data from the animal breeder for the period 1993-1995 demonstrated a mean post-implantation loss of 11.2% (based on results from 275 females) i.e. approx. 2-fold greater than the highest value obtained in the present study. Based on this information, the study director concludes that effects observed in the 300 mg/kg bwt/day group were unrelated to treatment. Effects recorded at 600 and 1000 mg/kg bwt/day while statistically significant were of doubtful toxicological relevance. The Reviewer agrees with this interpretation.

LITTER DATA
The total number of live fetuses was: 384, 360, 362, 352 (non-sig.)
The total number of litters was: 24, 24, 24, 23 (non-sig.)

The total number of fetuses and the number of live fetuses per litter was decreased significantly in the 600 and 1000 mg/kg bwt/day groups when expressed as a proportion of the total number of implantation sites.

Total fetuses (% implantation sites):
- per group : 98.5, 96.0 (P<0.05), 94.0 (P<0.01), 93.4 (P<0.01)
- per litter: 98.4, 95.7, 93.9 (P<0.05), 93.9 (P<0.01)

Live fetuses (% of implantation sites)
- per group: 98.2, 96.0, 94.0 (P<0.001), 93.4 (P<0.001)
- per litter: 98.1, 95.7, 93.9 (P<0.05), 93.9 (P<0.05)

Comment: Historical laboratory control data (based on litters from 117 females) included the report demonstrates that the concurrent control data were at the lower end of the control range:
- Total fetuses (%): mean = 96.9, SD = 2.6, 95% CI = 94.2-99.6
- Live fetuses (%): mean = 96.9, SD = 2.6, 95% CI = 94.2-99.6
The study director concludes that all values from the current study were within the background control range.

FETAL FINDINGS
Sex ratios were comparable between the groups (no significant differences). Fetal body weight was significantly decreased in litters from dams given 1000 mg/kg bwt/day only when calculated on a group basis. The study director notes this difference is of doubtful toxicological significance:
- all fetuses (g): 5.4, 5.3, 5.3, 5.3 (P<0.01)
- males (g): 5.5, 5.5, 5.5, 5.4 (P<0.05)
- females (g): 5.2, 5.2, 5.2, 5.2

EXTERNAL, VISCERAL AND SKELETAL EXAMINATION
No treatment-related external (macroscopic) changes were recorded. Visceral anomalies present in fetuses from the control and 1000 mg/kg bwt/day groups were consistent with spontaneous findings for rats of this strain. More complex morphological changes were present in one control and one high dose fetus, but these were isolated with no evidence of any relationship to treatment. There were no consistent differences in ossification parameters. Small numbers of fetuses from both the control and 1000 mg/kg bwt/day groups exhibited minor morphological changes but there was no evidence of any treatment related effect.

Test substance: Identification: MP Diol Glycol
Source: ARCO Chemical Company, Newtown Square, PA, USA
Description: clear liquid
Lot No: Lot SC 970619J05
Purity: >98%
Storage conditions: Room temperature, tightly closed container in the dark
Expiry date: 17 October 1998

Conclusion: No maternal toxicity was observed in female Wistar rats given MP Diol by oral gavage at dose levels of 300, 600 or 1000 mg/kg during pregnancy (GD 0-20). A statistically significant in embryonic (early) resorption was noted at 600 and 1000 mg/kg bwt/day, but the values were within the historical range for the laboratory and considered of doubtful toxicological relevance by the study director and also by an independent external reviewer. There was no evidence of any effect of treatment on morphological development or skeletal ossification. Based on these findings, the maternal and fetal NOAEL from this study was 1000 mg/kg bwt/day.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

09-NOV-2003 (37)

Species: rat **Sex:** female
Strain: Wistar
Route of administration: gavage
Exposure period: GD 0-19
Frequency of treatment: daily
Doses: 0, 100, 300 or 1000 mg/kg bwt/d
Control Group: other: yes (reverse osmosis water)
NOAEL Maternal Toxity: = 1000 mg/kg bw
NOAEL Teratogenicity: = 1000 mg/kg bw
NOAEL Fetotoxicity : = 1000 mg/kg bw

Method: EPA OPPTS 870.3700
Year: 1999
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND MAINTANENCE
- Species and strain: rat, Crl:CD (SD)IGS BR (Charles River Laboratories, Raleigh, NC, USA)
- Age: 71 days on receipt
- Acclimation period: 21 d
- Housing: individually housed in suspended wire mesh cages
- Diet: Certified Rodent LabDiet 5002 (PMI Nutrition International Inc.), ad libitum
- Water: reverse osmosis-treated tap water, ad libitum
- Environment: controlled to 72 +/- 4 degrees F, 30-70% rel. humidity, 12 hr light/dark cycle, 10 air changes/hr

MATING
One female was placed with one resident breeding male overnight (n = 125 per sex) and checked each morning for evidence of mating (copulatory plug, presence of spermatozoa in vaginal smear). The animals were separated once mating was confirmed, and mating discontinued when a total of 100 pregnancies were confirmed. Pregnant females were randomly allocated to treatment groups: the first pregnant female was assigned to the control group, the second to the low dose group, the third to the mid dose group etc. This procedure continued until there were 25 pregnant females in each dose group. The day of mating was designated GD 0, when body weights were in a range 230-321 g.

TREATMENT
Test substance administered by oral gavage (stainless steel cannula; 5 ml/kg bwt) at dose levels of 0 (deionized water), 100, 300 or 1000 mg/kg bwt/d on GD 0-19 inclusive. Doses were based upon the most recently recorded individual body weight data.

PREPARATION OF DOSING SOLUTIONS
Dosing solutions were prepared weekly in deionized water vehicle to give target concentrations of 0, 20, 60 or 200 mg/ml, and stored at room temperature.

ANALYSIS OF DOSING SOLUTIONS
Three aliquots (upper, mid and lower stratum of each formulation) was analyzed by GC. Stability was determined over 17 days (room temperature).

MATERNAL OBSERVATIONS
Dams were observed twice daily (morning, afternoon) for morbidity or mortality. Individual clinical observations were recorded from GD 0-20, prior to dosing and 1 hr post dosing. Body weight and food intake were recorded daily on GD 0-20.

NECROPSY
Dams were subject to a post-mortem examination on GD 20 (euthanized with carbon dioxide). The thoracic, abdominal and pelvic cavities were examined for macroscopic abnormalities. The ovaries and uterus were removed and examined for:
- number of corpora lutea per ovary
- weight of (trimmed) gravid uterus
- number and location of all fetuses, early and late resorptions and total number of implantation sites

Uteri with no macroscopic evidence of nidation were excised, opened and examined for early implantation losses (10% ammonium sulfide; Salewski (1964) Naunyn-Schm Archiv fur Exper Path und Pharm, 247, 367).

FETAL DATA
Each fetus was sexed, weighed and subject to a visceral examination (including heart and major blood vessels; Stuckhardt and Poppe (1984) Terat, Carc, Mutagen, 4, 181-188).

Heads from approx. one-half of the fetuses per litter were fixed (Bouin's solution) for subsequent soft tissue examination (Wilson (1965) In: Teratology - Principles and Techniques; Wilson and Warkany, ed, University of Chicago Press, pp 251-277); the remaining heads were examined by a mid-coronal slice.

All carcasses were eviscerated, fixed (100% ethanol) and stained with alizarin red S (Dawson (1926) Stain Technol, 1, 123-124) and alcian blue (Inouye (1976) Cong Anom 16, 171-173).

Crown-rump measurements were recorded for late resorptions, if present.

REPRODUCTION DATA
Data were collected to assess the following endpoints:
- fetal sex and weight
- number of fetuses (viable, dead)
- resorptions (early, late, total)

- number of implantation sites
- pre- and post implantation loss

STATISTICAL METHODS
Interuterine data per litter, fetal malformations and developmental variations per litter: Kruskal-Wallis test with Mann-Whitney U test
All other continuous data: One-way ANOVA with Dunnett's test

Result:

ANALYSIS OF DOSING SOLUTIONS
Results of periodic concentration analyses (n=4/dose level) returned the following mean concentrations:

-----mg/ml-----		
Target	Actual	SD
20	20.2	0.37
60	60.8	1.05
200	199	7.0

All results are presented by dose level (control, 300 mg/kg bwt, 600 mg/kg bwt, 1000 mg/kg bwt)

MATERNAL EFFECTS
All dams survived until scheduled necropsy on GD 20.

Clinical signs present in the treated group also occurred in the control group, with no indication of treatment-related changes.

There were no statistically significant differences in body weight or body weight gain. A single statistically significant decrease in food consumption in the 100 mg/kg bwt/day group (GD 12-13) appeared to be a spontaneous event, unrelated to treatment.

Net maternal body weight and net body weight gain (i.e. body weight on GD0 to GD20 minus gravid uterus weight) were comparable in all groups:
- net body weight (g): 340.1, 333.4, 336.5, 337.6
- net body weight gain (g): 69.0, 63.8, 66.9, 64.9

No macroscopic abnormalities were present at necropsy.

MATERNAL REPRODUCTION DATA
There was no statistically significant difference in the number of females that were pregnant and delivered litters : 24, 23, 25, 24

The pre-implantation loss in the 1000 mg/kg bwt/day group was numerically greater than in the controls (not statistically significant) due to complete resorption in one dam (no. 12440):
- pre-implantation loss (mean per group): 1.7, 2.2, 2.5, 3.1
- pre-implantation loss (% per litter): 8.8, 11.1, 12.6, 15.6

Comment: the result for the 1000 mg/kg bwt/day group was within the historical range (2.8-25.4%) for the laboratory and considered unrelated to treatment by the study director. When data for dam 12440 were excluded, the mean pre-implantation loss for the 1000 mg/kg bwt/day group was 12.4% per litter.

Post-implantation losses were unaffected by treatment:
- post-implantation loss (mean per group): 1.0, 1.0, 0.4, 0.8
- post-implantation loss (% per litter): 5.7, 6.0, 2.5, 8.4

There were no late resorptions in any of the control or treated groups, and no difference in number of corpora lutea or implantation sites.

LITTER DATA
The total number of live fetuses was: 397, 352, 403, 383 (non-sig.)
The total number of litters was: 24, 23, 25, 24 (non-sig.)

Interuterine growth and survival were unaffected by treatment with the test substance at any dose level:

Mean live litter size was unaffected by treatment; there were no dead fetuses:
- viable fetuses (mean per group): 16.5, 15.3, 16.1, 15.3
- viable fetuses (% per litter): 94.3, 94.0, 97.5, 91.6

FETAL FINDINGS
Sex ratios were comparable between the groups (no significant differences).

Body weight
Mean fetal weight was unaffected by treatment:
- all fetuses (g): 3.5, 3.5, 3.5, 3.5
- males (g): 3.6, 3.5, 3.6, 3.5
- females (g): 3.4, 3.4, 3.4, 3.4

EXTERNAL, VISCERAL AND SKELETAL EXAMINATION
Malformations were observed in 2(2), 0(0), 1(1) and 0(0) fetuses (litters), and considered by the study director to be of spontaneous origin.

No soft tissue malformations or developmental variations were observed at any dose level.

There were no consistent treatment-related differences in ossification parameters. The main variants were unossified sternebrae, ossified cervical centrum and rudimentary ribs but no evidence of any treatment related effect.

Test substance: Identity: MP Diol Glycol
Source: Lyondell Chemical Worldwide Inc, Newtown Square, PA, USA.

Lot: ACX 81019-1846
Purity: 98.7% by weight

Conclusion: No maternal toxicity was observed in female Wistar rats given MP Diol by oral gavage at dose levels of 100, 300, or 1000 mg/kg during pregnancy (GD 0-19). Interuterine growth and survival was unaffected by administration of the test substance at any dose level. There was no evidence of any effect of treatment on malformation or developmental variations of soft or skeletal tissue. Based on these findings, NOAEL for maternal toxicity, fetotoxicity and teratogenic effects was 1000 mg/kg bwt/day.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

09-NOV-2003 (32)

Species: rabbit **Sex:** female
Strain: New Zealand white
Route of administration: gavage
Exposure period: GD 0-28
Frequency of treatment: daily
Doses: 0, 250, 500 or 1000 mg/kg bwt/d
Control Group: other: yes (deionized water)
NOAEL Maternal Toxity: = 1000 mg/kg bw
NOAEL Teratogenicity: = 1000 mg/kg bw
NOAEL Fetotoxicity : = 1000 mg/kg bw

Method: EPA OPPTS 870.3700
Year: 2003
GLP: yes
Test substance: as prescribed by 1.1 - 1.4

Method: ANIMALS AND MAINTANENCE
- Species and strain: rabbit, New Zealand white (Covance Research Products Inc., Denver, PA, USA)
- Age: approx. 5.5 mo on receipt
- Acclimation period: 19 d
- Housing: individually housed in suspended wire mesh cages
- Diet: Certified Rabbit LabDiet 5322 (PMI Nutrition International Inc.), ad libitum
- Water: reverse osmosis-treated tap water, ad libitum
- Environment: controlled to 72 +/- 4 degrees F, 30-70% rel. humidity, 12 hr light/dark cycle, 10 air changes/hr

MATING
Females were artificially inseminated with sperm from 17 resident breeding male NZW rabbits. Immediately after insemination, does were administered human gonadotrophic hormone (Novarel, 100 USP units) via the marginal ear vein to induce ovulation. The day of insemination was designated GD 0.

TREATMENT

The test substance was administered undiluted using a 12-gauge stainless steel dosing needle, using dose volumes of 0.25, 0.50 or 1.0 ml/kg bwt (equiv. to 250, 500 or 1000 mg/kg bwt/d).

ANALYSIS
A sample of test substacne was analyzed by GC prior to first dosing and after the study was completed. Purity was established as >99.43% with no degradation over the course of the investigation.

MATERNAL OBSERVATIONS
Does were observed twice daily (morning, afternoon) for morbidity or mortality. Individual clinical observations were recorded from GD 0-29, prior to dosing and 1 hr post dosing. Body weight and food intake were recorded daily on GD 0-29. Net body weight and net body weight change were calculated based upon maternal body weight at GD 29 minus the weight of the uterus and contents.

NECROPSY
Does were subject to a post-mortem examination on GD 29 (euthanized with sodium pentobarbital, iv). The thoracic, abdominal and pelvic cavities were examined for macroscopic abnormalities. The ovaries and uterus were removed and examined for:
- number of corpora lutea per ovary
- weight of (trimmed) gravid uterus
- number and location of all fetuses, early and late resorptions and total number of implantation sites

Uteri with no macroscopic evidence of nidation were excised, opened and examined for early implantation losses (10% ammonium sulfide; Salewski (1964) Naunyn-Schm Archiv fur Exper Path und Pharm, 247, 367).

Materinal tissues were preserved in 10% neutral-buffered formalin for possible microscopic examination.

FETAL DATA
Each fetus was subject to a macroscopic external examiniation (including the eyes, palate and external orifices), weighed and subject to a visceral examination (including heart and major blood vessels; Stuckhardt and Poppe (1984) Terat, Carc, Mutagen, 4, 181-188). Sex was determined by internal examination, while fetal kidneys were examined and graded for renal papillae development (Woo and Hoar (1972) Teratology, 6, 191).

Heads from all fetuses were examined by mid-coronal slice. All carcasses were eviscerated and fixed in 100% ethanol, followed by staining with Alizarin Red S (Dawson (1926) Stain Technol, 1, 123-124). External, visceral and skeletal findings were recorded as developmental variations or

malformations.

REPRODUCTION DATA
Data were collected to assess the following endpoints:
- fetal sex and weight
- number of fetuses (viable, dead)
- resorptions (early, late, total)
- number of implantation sites
- pre- and post implantation loss

STATISTICAL METHODS
Interuterine data per litter, fetal malformations and developmental variations per litter: Kruskal-Wallis test with Mann-Whitney U test.
Mean fetal weight (segregated by sex): nested analysis of covariance, with litter size as covariate.
All other continuous data: One-way ANOVA with Dunnett's test.

Result: All results are presented by dose level (control, 250 mg/kg bwt, 500 mg/kg bwt, 1000 mg/kg bwt)

MATERNAL EFFECTS
One mid-dose female (no. 37341; esophageal perforation) and two high-dose females (37313, 37324; improper gavage administration and/or aspiration into lungs) died on GD 28, 23 or 21, respectively. All other dams survived until scheduled necropsy on GD 29.

Clinical signs present in the treated group also occurred in the control group, with no indication of treatment-related changes.

There were no statistically significant differences in body weight or body weight gain.

Net maternal body weight and net body weight gain were comparable in all groups:
- net body weight (g): 3966, 3899, 3875, 3863
- net body weight gain (g): 217, 162, 135, 176

With the exception of findings recorded in does that died prematurely (see above), no treatment-related macroscopic abnormalities were present at necropsy.

MATERNAL REPRODUCTION DATA
There was no statistically significant difference in the number of females that were pregnant and delivered litters : 24, 23, 23, 20

Interuterine growth and survival (postimplantation loss, live litter size, fetal body weight, fetal sex ratio) were generally unaffected by treatment.

The proportion of postimplantation loss (early and late

resorptions) in the 1000 mg/kg bwt/d group was increased (16.9% per litter; non-significant) relative to the control group (8.2% per litter) and the historic control (9.0% per litter) groups. This was due to two females (nos. 37318, 37328) that had entirely resorbed litters. Because the mean litter proportion of postimplantation loss was only slightly elevated relative to the historic data and non-significantly increased relative to the concurrent controls, the study report concludes that this was unrelated to treatment with MP Diol Glycol.

LITTER DATA
The total number of live fetuses was: 147, 169, 155, 133 (non-sig.)
The total number of litters was: 24, 23, 23, 20 (non-sig.)

Mean live litter size was unaffected by treatment; there were no dead fetuses:
- viable fetuses (mean per group): 6.1, 7.3, 6.7, 6.7
- viable fetuses (% per litter): 92, 96, 93, 90

FETAL FINDINGS
Sex ratios were comparable between the groups (no significant differences).

Body weight
Nested analysis of covariance indicated that fetal body weight was reduced significantly for males from the 500 mg/kg bwt/d group (decreased 7.2% relative to control) and for males and combined sexes in the 1000 mg/kg bwt/d groups (reduced 11.1% and 11.5%, respectively).
- male fetal weight (g): 50.3, 47.5, 46.7 (P,0.05), 44.7 (P<0.05)
- female fetal body weight (g): 48.9, 45.8, 45.7, 44.3
- combined fetal weights (g): 50.3, 46.6, 46.2, 44.5 (P<0.05)
The study report notes that these values were, however, within the historic range for the laboratory (39.9-51.7 g males, 39.2-51.8 g combined) and these reductions were therefore considered unrelated to treatment.

EXTERNAL, VISCERAL AND SKELETAL EXAMINATION
External malformations were present in one control (open eyelid) and one 1000 mg/kg bwt/d (spina bifida) fetus, but were considered unrelated to treatment by the study director. There were no external developmental variations.

Soft tissue malformations were observed in one fetus each from the 500 mg/kg bwt/d (malpositioned kidney) and 1000 mg/kg bwt/d (lateral transposition of major and great vessels, abnormal lung lobation) but were considered unrelated to treatment by the study director. Soft tissue developmental variations were comparable in the control and treated groups.

Skeletal malformations were observed in 1(1), 4(4) and 4(3) fetuses (litters). Severe malalignment of one or more or the sternebrae was observed in one fetus from the low and mid dose groups, and two from the high dose group (same litter) however these findings were not statistically significant. Fused sternebrae or vertebral anomalies (with or without associated rib anomalies) were seen in one or two fetuses from all treated litters, however the findings were non statistically significant relative to the controls and no dose relationship was apparent. Skeletal developmental variations occurred similarly in control and treated litters.

Test substance: Identification: MP Diol Glycol
Source: Lyondell Chemical Company. the Netherlands
Description: clear, colorless liquid
Lot No: RBMPD_3727
Purity: >99.43%
Storage conditions: Room temperature, closed bottle

Conclusion: No maternal toxicity was observed in New Zealand white rabbits given MP Diol by oral gavage at dose levels of 250, 500 or 1000 mg/kg during pregnancy (GD 0-29). Interuterine growth and survival was unaffected by administration of the test substance at any dose level. There was no evidence of any effect of treatment on malformation or developmental variations of soft or skeletal tissue. Based on these findings, NOAEL for maternal toxicity, fetotoxicity and teratogenic effects was 1000 mg/kg bwt/day.

Reliability: (1) valid without restriction
Study report available for review, GLP-compliant guideline investigation with clear reporting of methods and tabulation of findings in data tables and appendices.

16-NOV-2003 (34)

5.8.3 Toxicity to Reproduction, Other Studies

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5.9 Specific Investigations

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5.10 Exposure Experience

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5.11 Additional Remarks

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6.1 Analytical Methods

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6.2 Detection and Identification

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7.1 Function

-

7.2 Effects on Organisms to be Controlled

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7.3 Organisms to be Protected

-

7.4 User

-

7.5 Resistance

-

8.1 Methods Handling and Storing

-

8.2 Fire Guidance

-

8.3 Emergency Measures

-

8.4 Possib. of Rendering Subst. Harmless

-

8.5 Waste Management

-

8.6 Side-effects Detection

-

8.7 Substance Registered as Dangerous for Ground Water

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8.8 Reactivity Towards Container Material

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(1) Armstrong, T (2003) MP Diol Fate and Transport Modeling. Unpublished memo and attachments, BBL Inc For Lyondell Chemical Company, 27 June 2003.

(2) Armstrong, T (2003) MP Diol Glycol Bioaccumulation Model. Unpublished memo and attachments, BBL Inc For Lyondell Chemical Company, 1 December 2003.

(3) Armstrong, T (2003) MPDiol Photodegradation. Unpublished memo and attachments, BBL Inc For Lyondell Chemical Company, 18 November 2003.

(4) Boatman, RJ and Lantum, HMB (2003) Metabolism and disposition of [2-14C]-2-methyl-1,3-propanediol (MPDiol) in Sprague-Dawley rats following oral gavage administration. Eastman Kodak Company draft Report TX-2003-092, unpublished study for Lyondell Chemical Co.

(5) Bogers, M (1993) 96-hour acute toxicity study in the Carp with MP Diol Glycol. RCC NOTOX Project 091755. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(6) Bogers, M (1993) Activated sludge respiration inhibition test with MP Diol Glycol. RCC NOTOX Project 091776. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(7) Bogers, M (1993) Ready biodegradability: modified Sturm test with MP Diol Glycol. RCC NOTOX Project 091777. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(8) Bogers, M (1993) Scenedesmus subspicatus; fresh water algal growth inhibition test with MP Diol Glycol. RCC NOTOX Project 091801. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(9) Cerven, DR (1988) Acute dermal toxicity in rabbits/LD50 in rabbits. MB Research Laboratories Project MB 88-9013B. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(10) Cerven, DR (1988) Eye irritation in rabbits. MB Research Laboratories Project MB 88-9013D. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(11) Cerven, DR (1988) Primary Dermal irritation in rabbits. MB Research Laboratories Project MB 88-9013C. Unpublished report for Lyondell Chemical Worldwide Inc, Newtown Square, PA.

(12) Cerven, DR (1988) Single dose oral toxicity in rats/LD50 in rats. MB Research Laboratories Project MB 88-9013A. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(13) Daamen, PAM (1993) Assessment of contact hypersensitivity to MP Diol Glycol in the albino guinea pig (maximization test). RCC NOTOX Project 091687. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(14) de Vries, R (1993) Determination of the partition coefficient (n-octanol/water) of MP Diol Glycol (flask-shaking method). RCC NOTOX Project 091621. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(15) de Vries, R (1993) Determination of the vapour pressure of MP Diol Glycol. RCC NOTOX Project 091586. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(16) de Vries, R (1993) Determination of the water solubility of MP Diol Glycol. RCC NOTOX Project 091608. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(17) Desmares-Koopmans, MJE (1998) Ready biodegradability: closed bottle test with MP Diol Glycol. NOTOX Project 213582. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(18) Eisenberg, RR (1997) 14 Day cumulative irritation test (ProtocolNo. 1.04). Consumer Product testing Co. Project C97-0313. Unpublished report for Lyondell Chemical Company, Newtown Square, PA.

(19) Eisenberg, RR (1997) Repeated insult patch test (Protocol No. 1.01) with MP Diol Glycol; retest of MP Diol Glycol reactors with propylene glycol and 1,3-butylene glycol. Consumer Product testing Co. Project C97-0156. Unpublished report for Lyondell Chemical Company, Newtown Square, PA.

(20) Eisenberg, RR (1999) Repeated insult patch test (Protocol No. 1.01): MP Diol (796047B) (occluded). Consumer Product testing Co. Project C99-0968.03. Unpublished report for Lyondell Chemical Company, Newtown Square, PA.

(21) Eisenberg, RR (1999) Repeated insult patch test (Protocol No. 1.01): MP Diol (796047B) (semi). Consumer Product testing Co. Project C99-0968.04. Unpublished report for Lyondell Chemical Company, Newtown Square, PA.

(22) Eisenberg, RR (1999) Repeated insult patch test (Protocol No. 1.01): MP Diol LO (796047A) (occluded). Consumer Product testing Co. Project C99-0968.01. Unpublished report for Lyondell Chemical Company, Newtown Square, PA.

(23) Eisenberg, RR (1999) Repeated insult patch test (Protocol No. 1.01): MP Diol LO (796047A) (semi). Consumer Product testing Co. Project C99-0968.02. Unpublished report for Lyondell Chemical Company, Newtown Square, PA.

(24) Lee, KB and Aufderheide, JA (2003) Toxicity of MP Diol on emergence of seedlings and early stages of growth of terrestrial plants. ABC Laboratories Inc Project MB 47908. Unpublished report for Lyondell Chemical Company, Houston, TX.

(25) Lyondell Chemical Company (2002) EU Sales Specification for MP Diol Glycol (material No. 509247). Validation date 04/22/2002.

(26) Lyondell Chemical Company (2002) Material Safety Data Sheet for MP Diol Glycol, Ver. 1.3, Validation Date 03/15/2002.

(27) Lyondell Chemical Company (2002) US Sales Specification for MP Diol Glycol (material No. 499177). Validation date 04/22/2002.

(28) Meylan, WM and Howard, PH (1993) Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere 26: 2293-99.

(29) Meylan, WM, Howard, PH, Boethling, RS, Aronson, D, Printup, H and Gouchie, S (1999) Improved method for estimating bioconcentration/bioaccumulation factor from octanol/water partition coefficient. Environ. Toxicol. Chem. 18, 664-672.

(30) Mitchell, C (1993) Acute toxicity study in Daphnia magna with MP Diol Glycol. RCC NOTOX Project 091744. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(31) Muijser, H (1997) Acute (4-hour) inhalation toxicity study with MP Diol Glycol in rats. Notox Project No. 213569. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(32) Nemec, MD (1999) An oral (gavage) pre-natal developmental toxicity study of MP Diol Glycol in rats. Unpublished study WIL-14033, WIL Research Laboratories Inc., USA, for Lyondell Chemical Worldwide Inc.

(33) Nemec, MD (2000) An oral (gavage) two-generation reproductive toxicity study of MP Diol Glycol in rats. Unpublished study WIL-14034, WIL Research Laboratories Inc., USA, for Lyondell Chemical Company.

(34) Nemec, MD (2003) An oral (gavage) prenatal developmental toxicity study of MP Diol Glycol in rabbits. Unpublished study WIL-14036, WIL Research Laboratories Inc., USA, for Lyondell Chemical Company, Maidenhead, UK.

(35) Reijnders, JBJ (1993) Assessment of 90 day oral toxicity with MP Diol Glycol in the rat. Unpublished study 091711, NOTOX Safety and Environmental Research BV, the Netherlands, for ARCO Chemical Co.

(36) Reijnders, JBJ (1993) Subacute 14-day oral toxicity with MP Diol Glycol by daily gavage in the rat. Unpublished study 091709, NOTOX Safety and Environmental Research BV, the Netherlands, for ARCO Chemical Co.

(37) Reijnders, JBJ (1998) Embryotoxicity and teratogenicity study with MP Diol Glycol administered by oral gavage in Wistar rats. Unpublished study 213536, NOTOX Safety and Environmental Research BV, the Netherlands, for ARCO Chemical Co.

(38) Treur, J (1993) Determination of the UV-VIS absorption spectra of MP Diol Glycol. RCC NOTOX Project 091542. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(39) van der Waart, EJ (1993) Evaluation of the ability of MP Diol Glycol to induce chromosomal aberrations in cultured peripheral human lymphocytes (with independent repeat). RCC NOTOX Project 091733. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(40) van der Waart, EJ (1993) Evaluation of the mutagenic activity of MP Diol Glycol in an in vitro mammalian cell mutation test with V79 Chinese hamster cells (with independent repeat). RCC NOTOX Project 091722. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(41) van der Waart, EJ (1993) Evaluation of the mutagenic activity of MP Diol Glycol in the Ames Salmonella/microsome test (with independent repeat). RCC NOTOX Project 091722. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(42) van Helvoirt, JAMW (1993) Determination of the auto-flammability (liquids) of MP Diol Glycol . RCC NOTOX Project 091665. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(43) van Helvoirt, JAMW (1993) Determination of the boiling point/boiling range of MP Diol Glycol. RCC NOTOX Project 091564. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(44) van Helvoirt, JAMW (1993) Determination of the density (liquid) of MP Diol Glycol. RCC NOTOX Project 091565. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(45) van Helvoirt, JAMW (1993) Determination of the flammability (liquid) of MP Diol Glycol. RCC NOTOX Project 091643. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(46) van Helvoirt, JAMW (1993) Determination of the flash point of MP Diol Glycol. RCC NOTOX Project 091632. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(47) van Helvoirt, JAMW (1993) Determination of the freezing point/freezing range of MP Diol Glycol. RCC NOTOX Project 091553. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

(48) van Helvoirt, JAMW (1993) Determination of the surface tension of an aqueous solution of MP Diol Glycol. RCC NOTOX Project 091597. Unpublished report for ARCO Chemical Company, Newtown Square, PA.

10.1 End Point Summary

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10.2 Hazard Summary

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10.3 Risk Assessment

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